EPIDEMIOLOGY & ETIOLOGY OF CHRONIC KIDNEY DISEASE

By

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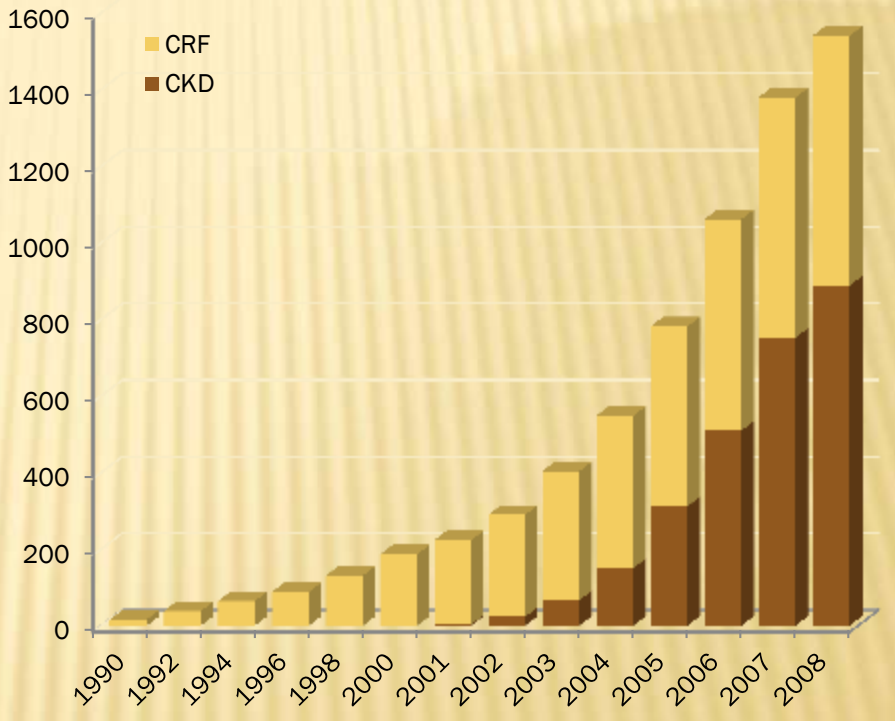
Growing Interest

Medline publications 1998-2008

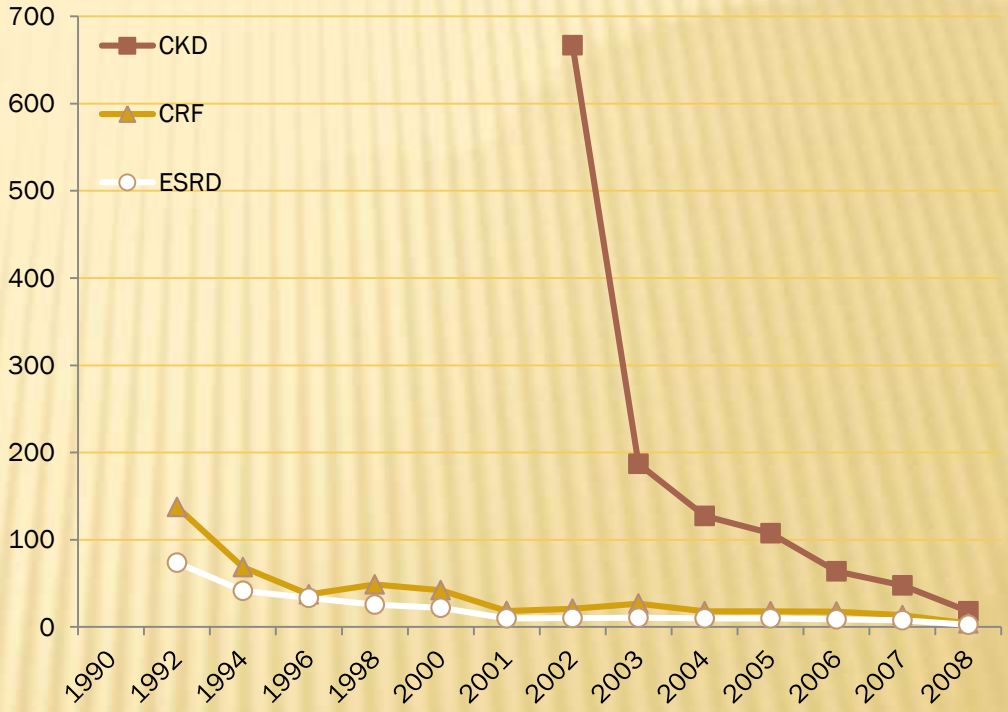


Same, excluding ESRD

Pubmed database, accessed 7th July 2008

Growing Interest

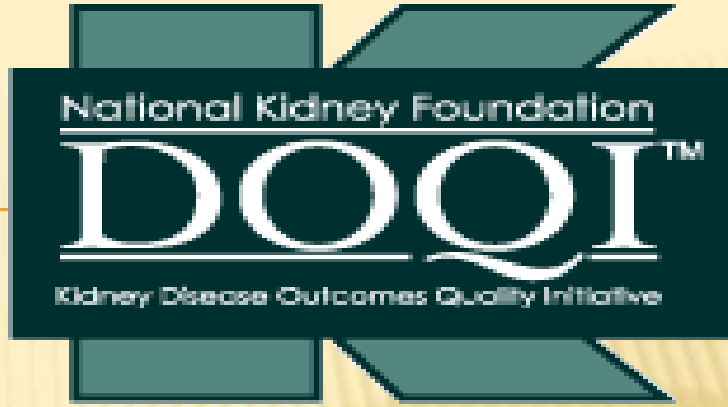
- The growing ESRD dilemma
- The recent focus on earlier stages renal disease
- Relationship of CKD to CVD
- Identification of tools for the prevention and treatment of CKD



Percentage growth

Barsoum. N Engl J Med. 2006;354:997-9.

DEFINITION

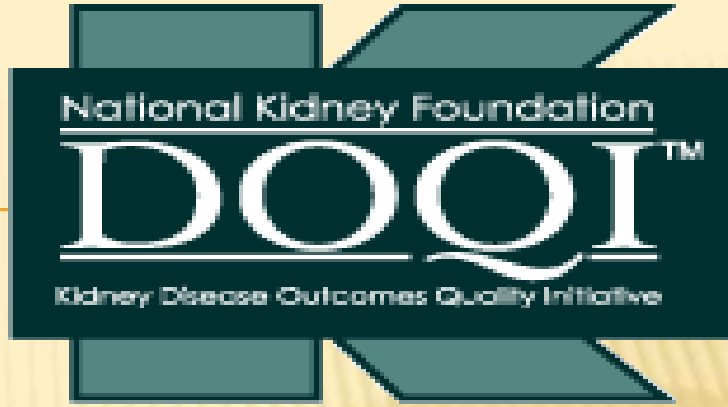


- Markers of kidney damage for ≥3 months ± decreased GFR:
  - Pathological abnormalities
  - Blood or urinary abnormalities
  - Imaging abnormalities

OR

- GFR < 60 mL/min/1.73 m^2 for ≥3 months ± other signs of kidney damage

CKD STAGING



Classification of CKD based on GFR as proposed by the Kidney Disease Outcomes Quality Initiative (K/DOQI) guidelines

CKD Stage	Description
1	Normal or increased GFR; some evidence of kidney damage reflected by microalbuminuria/proteinuria, hematuria, or histologic changes
2	Mild decrease in GFR (89–60 ml/min/1.73 m^2)
3	Moderate decrease in GFR (59–30 ml/min/1.73 m^2)
4	Severe decrease in GFR (29–15 ml/min/1.73 m^2)
5	GFR < 15 ml/min/1.73 m^2; when renal replacement therapy in the form of dialysis or transplantation has to be considered to sustain life

National Kidney Foundation: KDOQI kidney disease outcome quality initiative
Am J Kidney Dis 2002;39 (Supp 1) S1 – S266

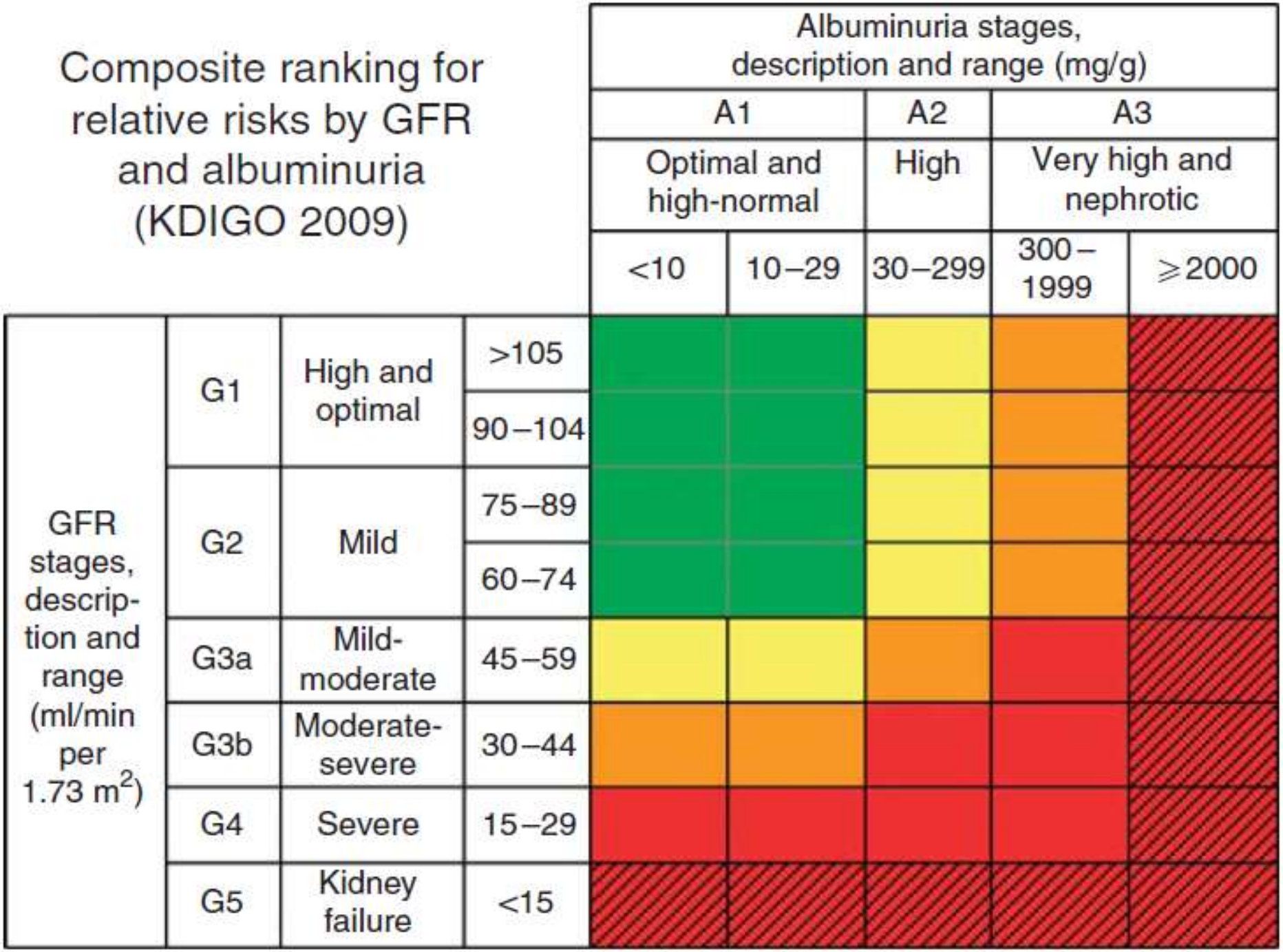
Stage	Description	Classification by Severity	Classification by Treatment
1	Kidney damage with normal or ↑ GFR	GFR ≥ 90	T if kidney transplant recipient
2	Kidney damage with mild ↓ in GFR	GFR of 60-89	
3	Moderate ↓ in GFR	GFR of 30-59	
4	Severe ↓ in GFR	GFR of 15-29	
5	Kidney failure	GFR < 15 (or dialysis)	D if dialysis

National Institute for Health and Clinical Excellence

CKD Stage	Definition
1	Normal or increased GFR; some evidence of kidney damage reflected by microalbuminuria, proteinuria, and hematuria as well as radiologic or histologic changes
2	Mild decrease in GFR (89–60 ml/min per 1.73 m^2) with some evidence of kidney damage reflected by microalbuminuria, proteinuria and hematuria as well as radiologic or histologic changes
3 3A 3B	GFR 59-30 ml/min per 1.73 m^2 GFR 59 to 45 ml/min per 1.73 m^2 GFR 44 to 30 ml/min per 1.73 m^2
4	GFR 29-15 ml/min per 1.73 m^2
5	GFR <15 ml/min per 1.73 m^2; when renal replacement therapy in the form of dialysis or transplantation has to be considered to sustain life
The suffix p to be added to the stage in proteinuric patients (proteinuria >0.5 g/24h)	

National Institute for Health and Clinical Excellence; September 2008.

Composite ranking for relative risks by GFR and albuminuria (KDIGO 2009)



FOCUS ON EARLY CKD

Broader Spectrum Of CKD

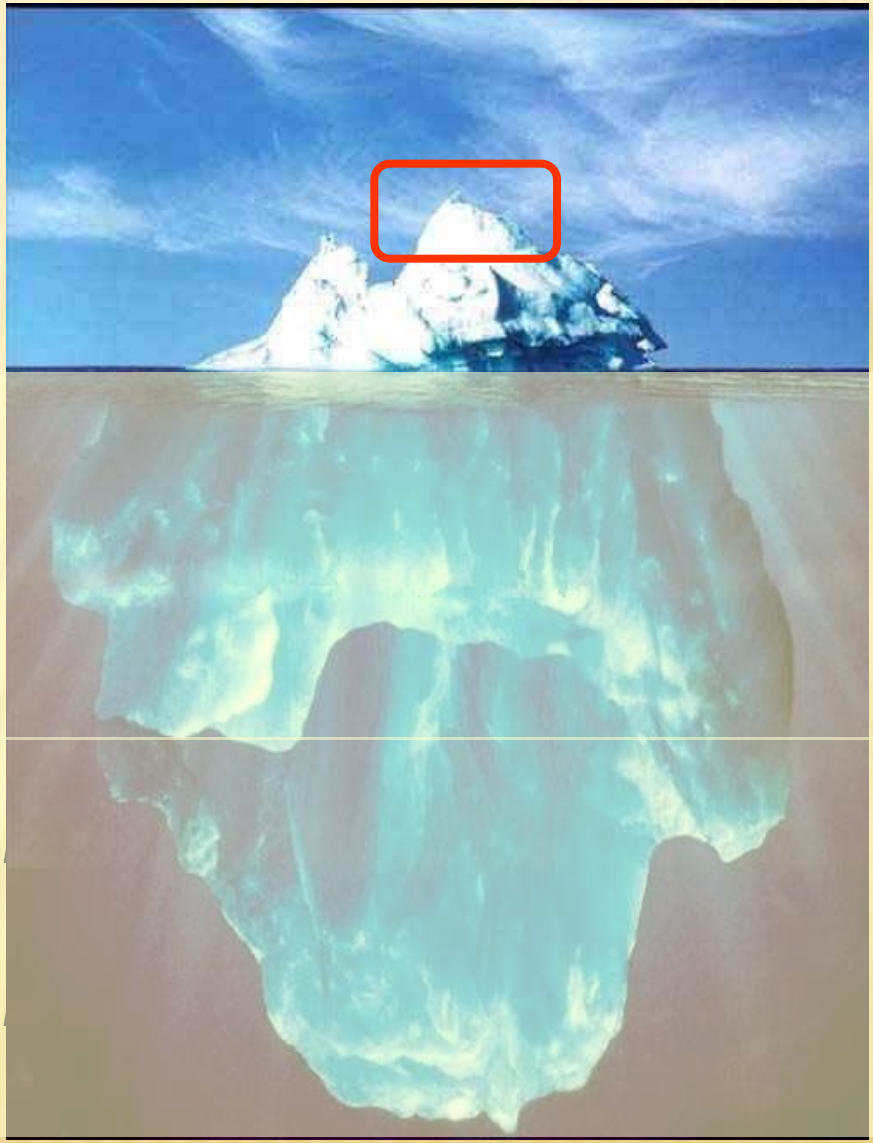
Severe CRF (ESRD)
Stage V
eGFR <15ml/min

Moderate CRF (Failure)
Stage IV
eGFR 15-29ml/min

Mild CRF (Insufficiency)
Stage III
eGFR 30-60ml/min

Stage II
Structural damage, eGFR >60ml

Stage I
Structural damage, eGFR >90ml



11.05 %

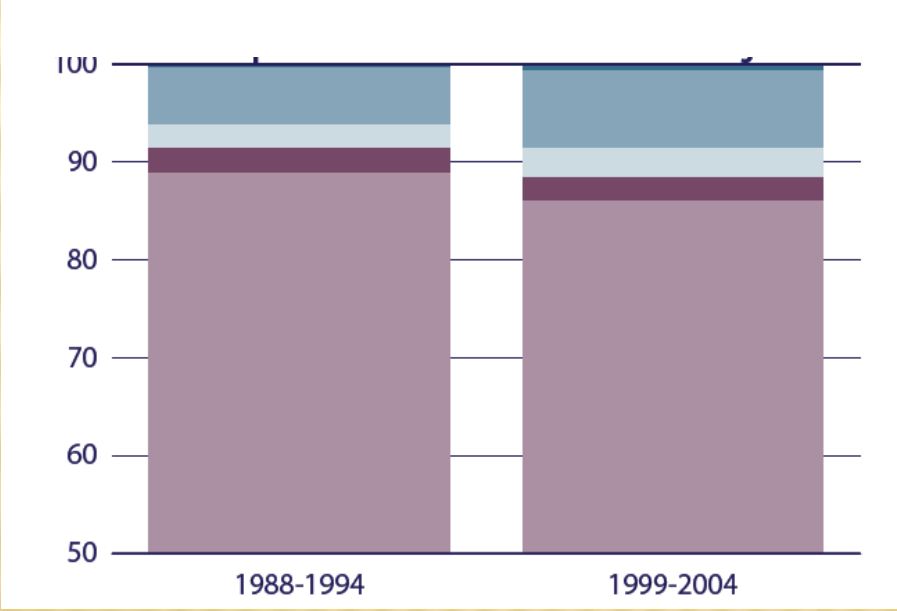
0.2	1
0.25	1.25
4.3	21.5
3.0	15.0
3.3	16.5

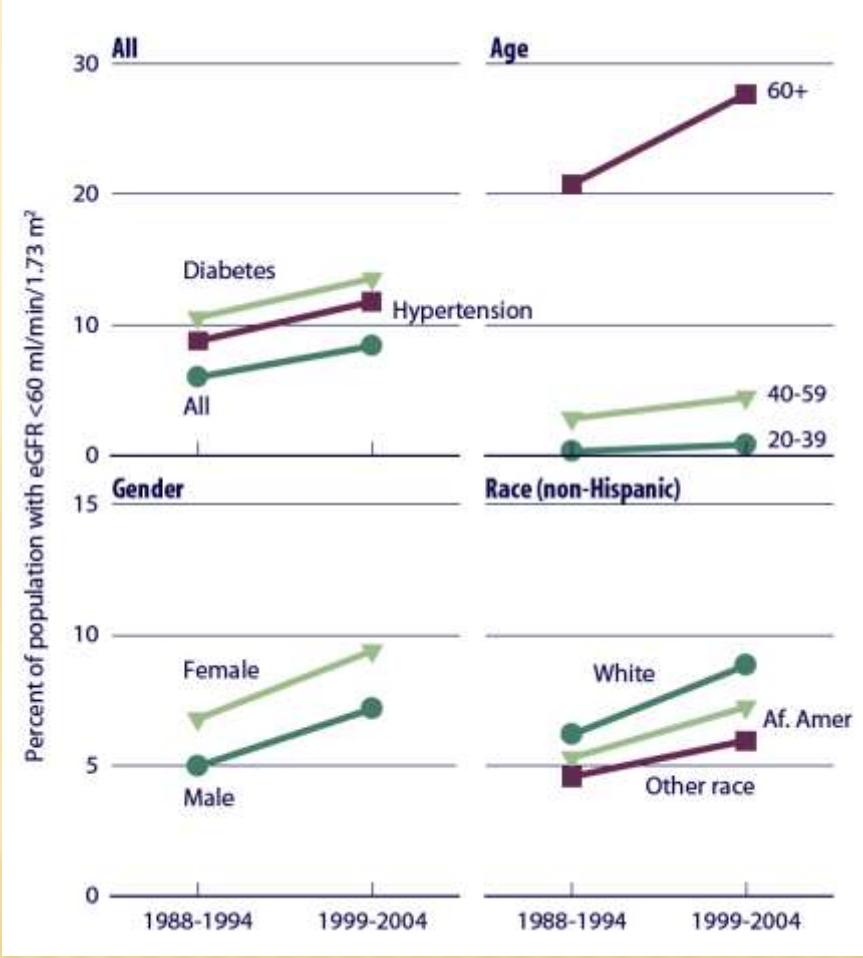
KDOQI 2002 *National Health and Nutritional Examination Survey* *NHANES III, 1988-1994*

Increasing Prevalence

Comparative NHANES III data

USRDS Annual report 2007





Europe

PREVEND Study
Gröningen, The Netherlands

- Community-based
- 40,548 subjects, 28-75 Y old
- Median follow up 961 days
- 7 % Proteinuria

Hillege et al. Circulation 2002;106(14):e9037-8.

Japan

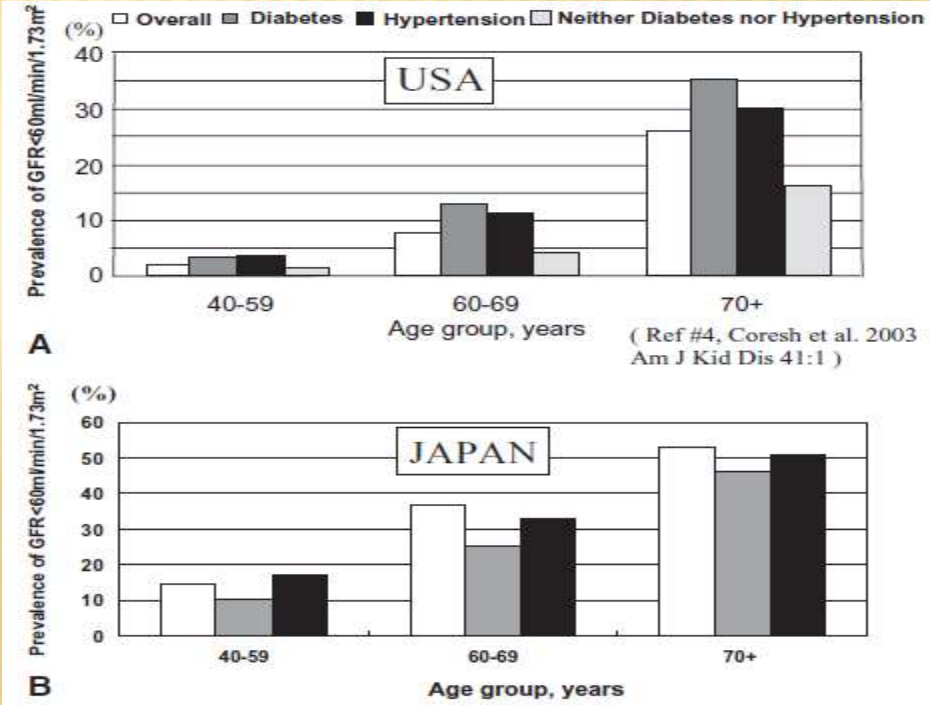
No national prevalence data

Imai et al. Clin Exp Nephrol. 2007;11:156-63

Kidney Disease Screening Program in Japan

- Community based
- 10-year study
- 120,727 subjects ≥40 Years old
- Study duration 10 years

Imai et al. Hypertens Res. 2008;31(3):433-41.



Australia

- South Australia
  - Ausdiab
    - 11,247 Participants
      - Renal impairment 9.7%
      - Hematuria 3.7%
      - Proteinuria 1.1 %

      Total **16%**

Chadban et al, JASN 2003; 14:S131-S138

Australian Aboriginals

- North Australia
  - Tiwi Aboriginals
    - 672 participants
      - Microalbuminuria: 31%
      - GFR < 60: 12%
      - Elevated s Creatinine: 10%

Hoy. NDT 2000;15:1293-1297

South America

Bolivia

14,082 “Healthy” subjects

Plata R et al. NDT 1998;13:3034-3036

MSU, Dipstick

- No Abnormalities 9821 (69.7%)
- Abnormal urine 4261 (30.3 %)

Confirmatory tests

- No abnormality 35%
- Abnormalities 65%

19.7%

Uruguay

96 first-degree relatives of patients on RDT: CKD in 6.24 %

Abstract WNC Rio 2007

India

Chennai

27,086 Individuals

20,986 Treated for diabetes and hypertension

6,100 New participants

eGFR <80 ml/min

$8.6/10^3$

$13.9/10^3$

P<0.005, RR 1.61

Mani MK. Kidney Int Suppl. 2005(94):S75-8.

Delhi

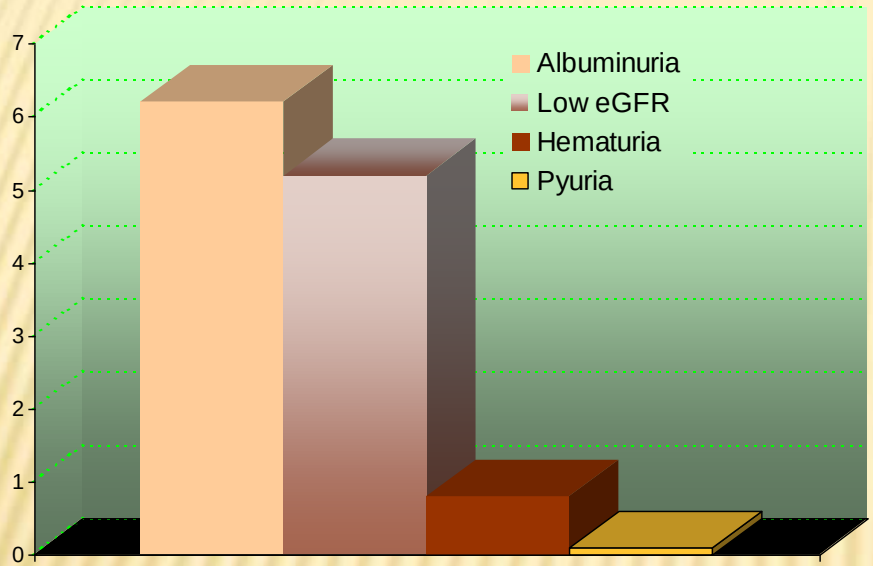
3,680 individuals: Proteinuria: 8.2 %, CKD >= Stage III: 7.93%

Abstract WCN Rio 2007

China

Beijing

2,353 individuals: 11.3% any evidence of CKD



Zhang et al. Nephrol Dial Transplant 2007;22:1093-9

Taiwan

1,811 individuals (17.4) % *Abstract WCN Rio 2007*

Africa

Reference	Country	Definition of CKD	Location	Results		
				Proteinuria (%)	Hypertension (%)	Uremia/Increased Creatinine (%)
Arogundade et al (2005)[10]	Nigeria	ESRD	Hospital based	—	—	8-16
Diouf et al (2000)[11]	Senegal	ESRD	Hospital based	—	—	33
Plange-Rhule et al[13]	Ghana	ESRD	Hospital based	—	—	5
Fogazzi et al (2003)[14]	Benin	Proteinuria/increased serum creatinine	Hospital based	1	—	3.3
Abioye-Kuteyi et al (1999)[18]	Nigeria	Proteinuria	Rural community	—	—	19.9
Asinobi et al (2007)[16]	Nigeria	Hypertension/ proteinuria	Urban community	2.9	28.2 (adults) 10.2 (children)	—

Arogundade & Barsoum. AJKD 2008; 51:515-523

Republic of the Congo

- CKD estimated as 3.3%

Krzesinsk et al. Nephrol Dial Transplant 2007; 22: 332–335

Egypt

EGIPT-CKD Project

Egypt Information, Prevention and Treatment of Chronic Kidney Disease:

359 first-degree relatives of ESRD patients

Questionnaire (Personal, family, life style)
Demographics
A/C ratio
HGB, Sugar, Cholesterol, Triglycerides
Creatinine, eGFR by MDRD

Proteinuria 21%
CKD >= Stage III 3.9%

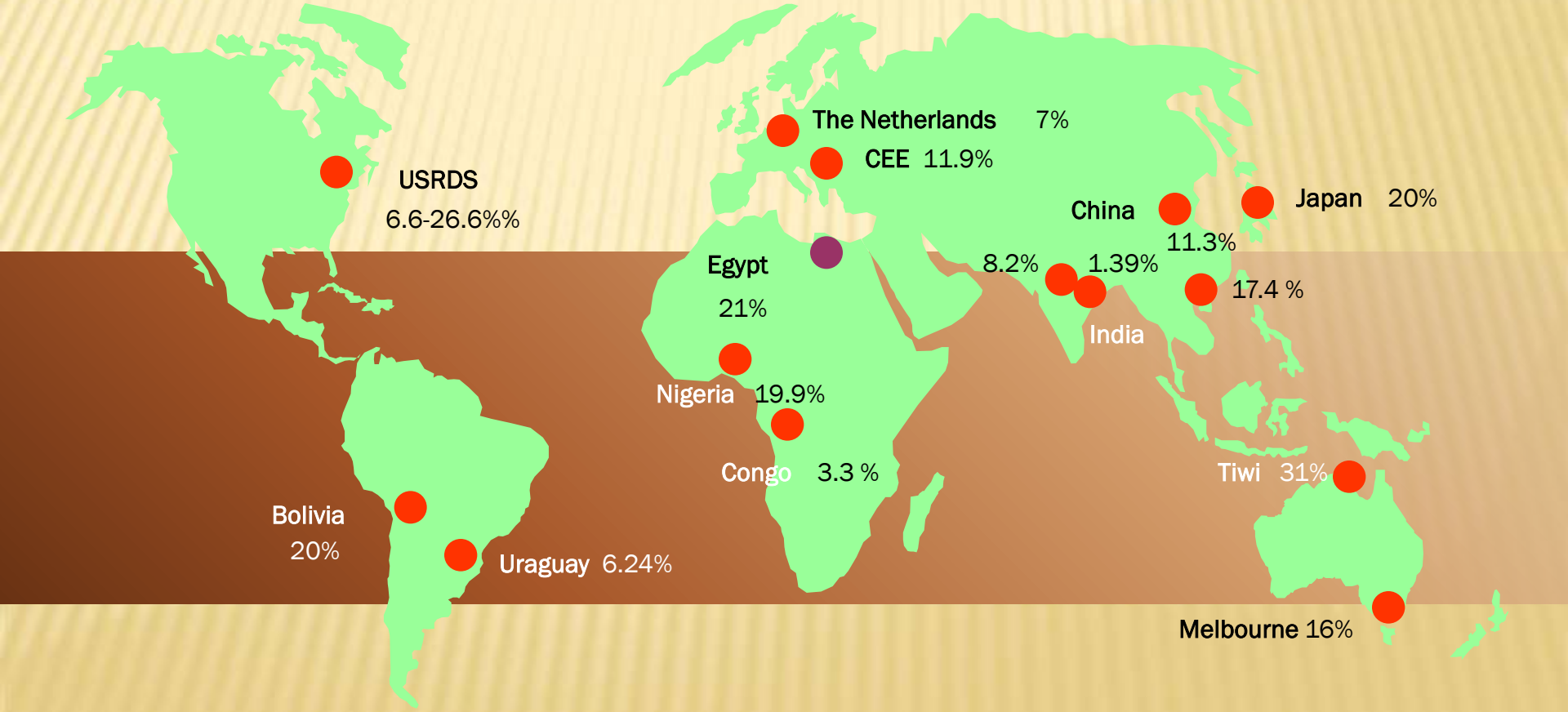
Global Outlook

Systematic review

Median 7.2 % >= 30 Y

23.4-35.8 % >= 64Y

Zhang & Rothenbacher BMC Public Health. 2008 ;11;8:117

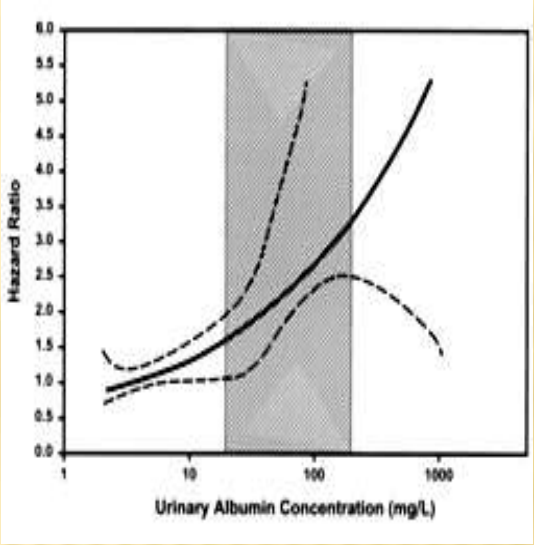


Potential Incidence Bias

Microalbuminuria

- Marker of endothelial injury
- Non-specificity
  - Diabetes
  - Obesity
  - Smoking
  - Exercise
  - Psoriasis
  - IBD
  - Other
- Reversibility

PREVEND



Bauer et al. JASN 2008;19(5):844-6.

MDRD

- Racial differences
  - Japanese factor
  - Chinese factor
  - Other populations

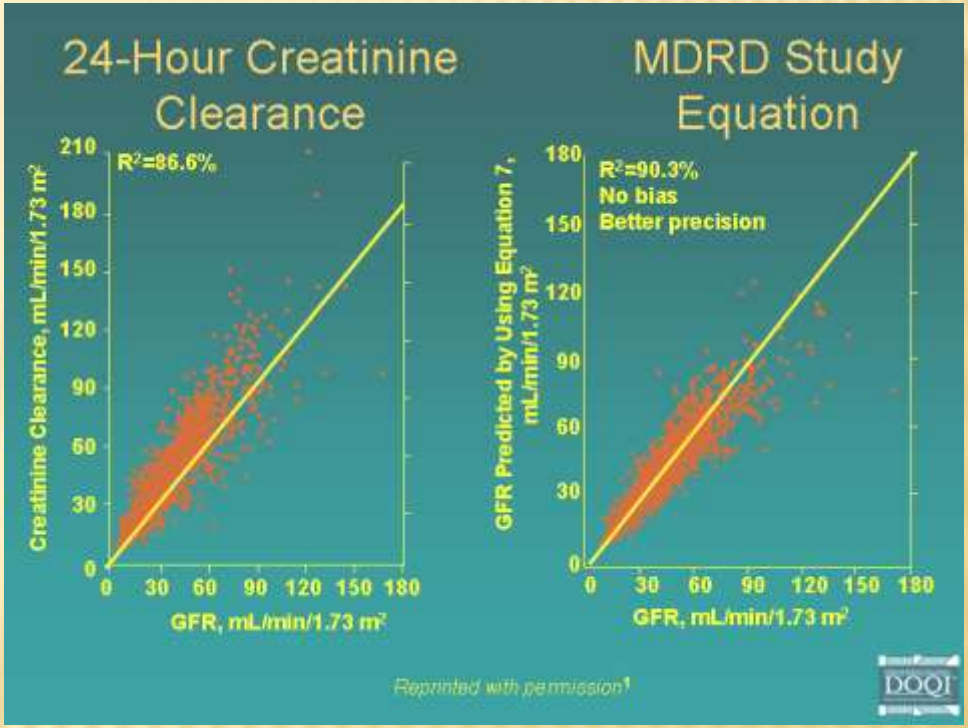
Kramer et al. CJASN 2008 Jun 11. [EAP]

- Range differences

Froissart, et al, JASN 2005;16:763–7

- Validity in AKI

- Fluctuation in old age



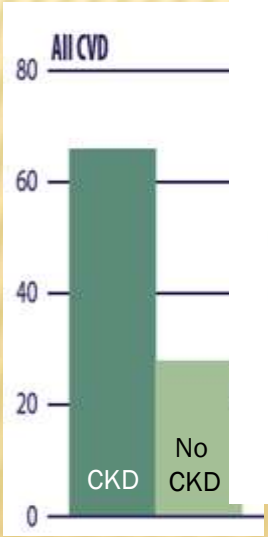
NATURAL HISTORY OF CKD

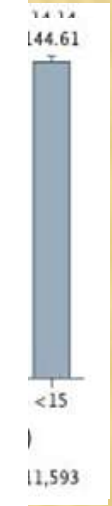
CKD Population Kinetics

Diabetes, hypertension, obesity, hyperlipidemia, metabolic syndrome, smoking, etc.

Table 2. Adjusted Hazard Ratio for Death from Any Cause, Cardiovascular Events, and Hospitalization among 1,120,295 Ambulatory Adults, According to the Estimated GFR.*

Estimated GFR	Death from Any Cause	Any Cardiovascular Event	Any Hospitalization
	adjusted hazard ratio (95 percent confidence interval)		
≥60 ml/min/1.73 m²†	1.00	1.00	1.00
45–59 ml/min/1.73 m²	1.2 (1.1–1.2)	1.4 (1.4–1.5)	1.1 (1.1–1.1)
30–44 ml/min/1.73 m²	1.8 (1.7–1.9)	2.0 (1.9–2.1)	1.5 (1.5–1.5)
15–29 ml/min/1.73 m²	3.2 (3.1–3.4)	2.8 (2.6–2.9)	2.1 (2.0–2.2)
<15 ml/min/1.73 m²	5.9 (5.4–6.5)	3.4 (3.1–3.8)	3.1 (3.0–3.3)





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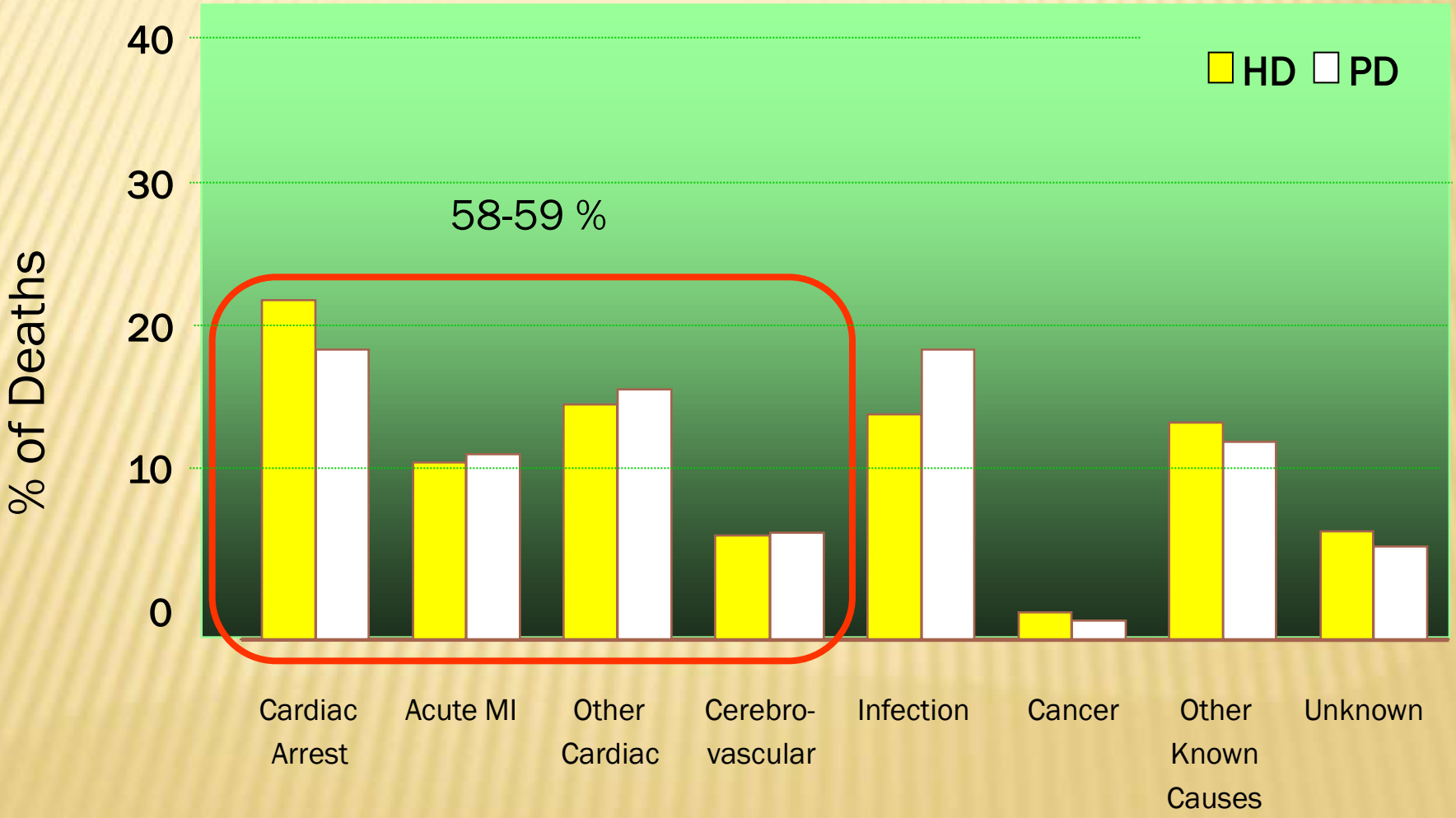
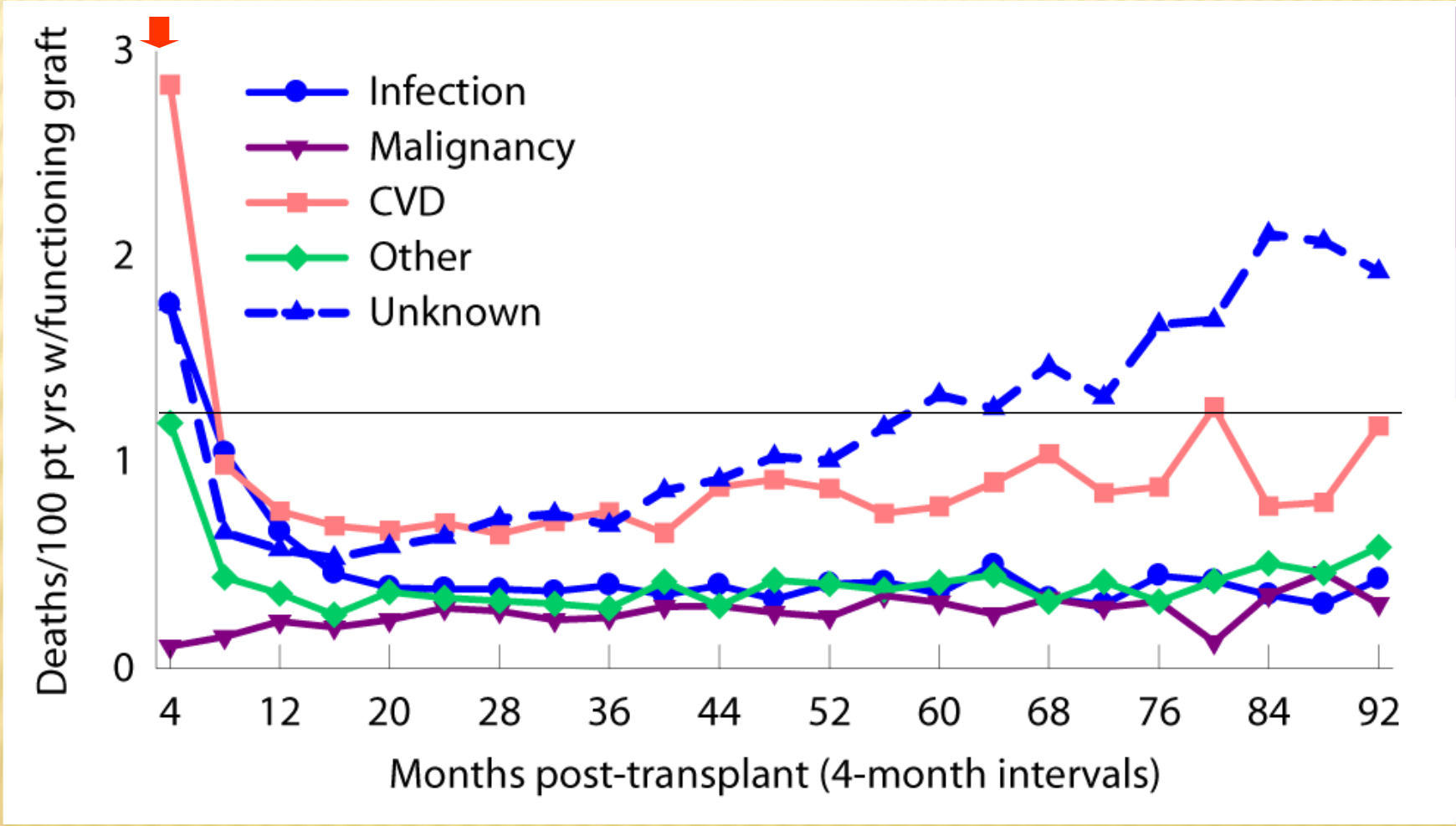
Go A et al. N Engl J Med 2004;351:1296-1305

Causes Of Death On Dialysis

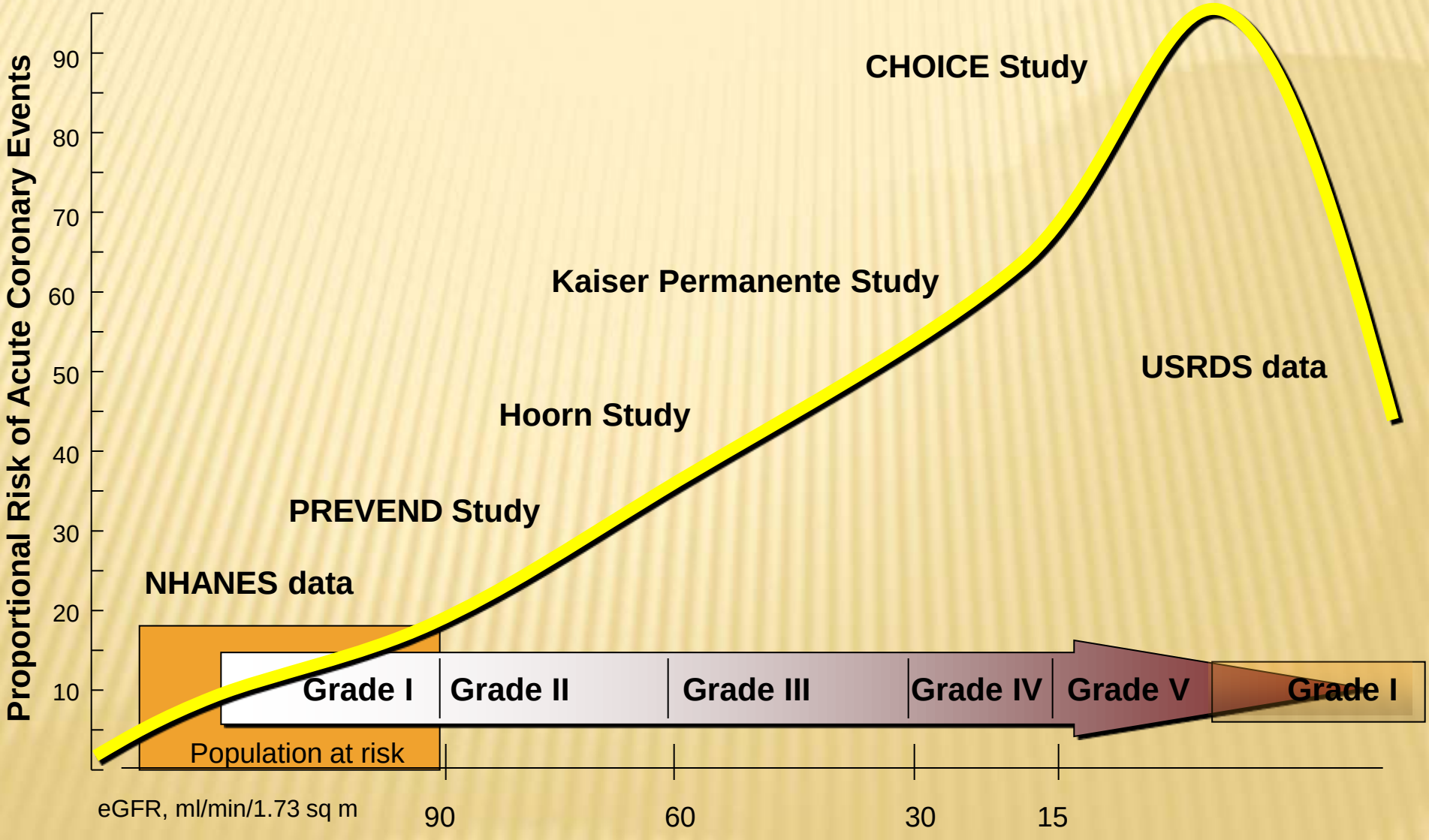


Causes Of Death In Transplant Recipients



USRDS 2005

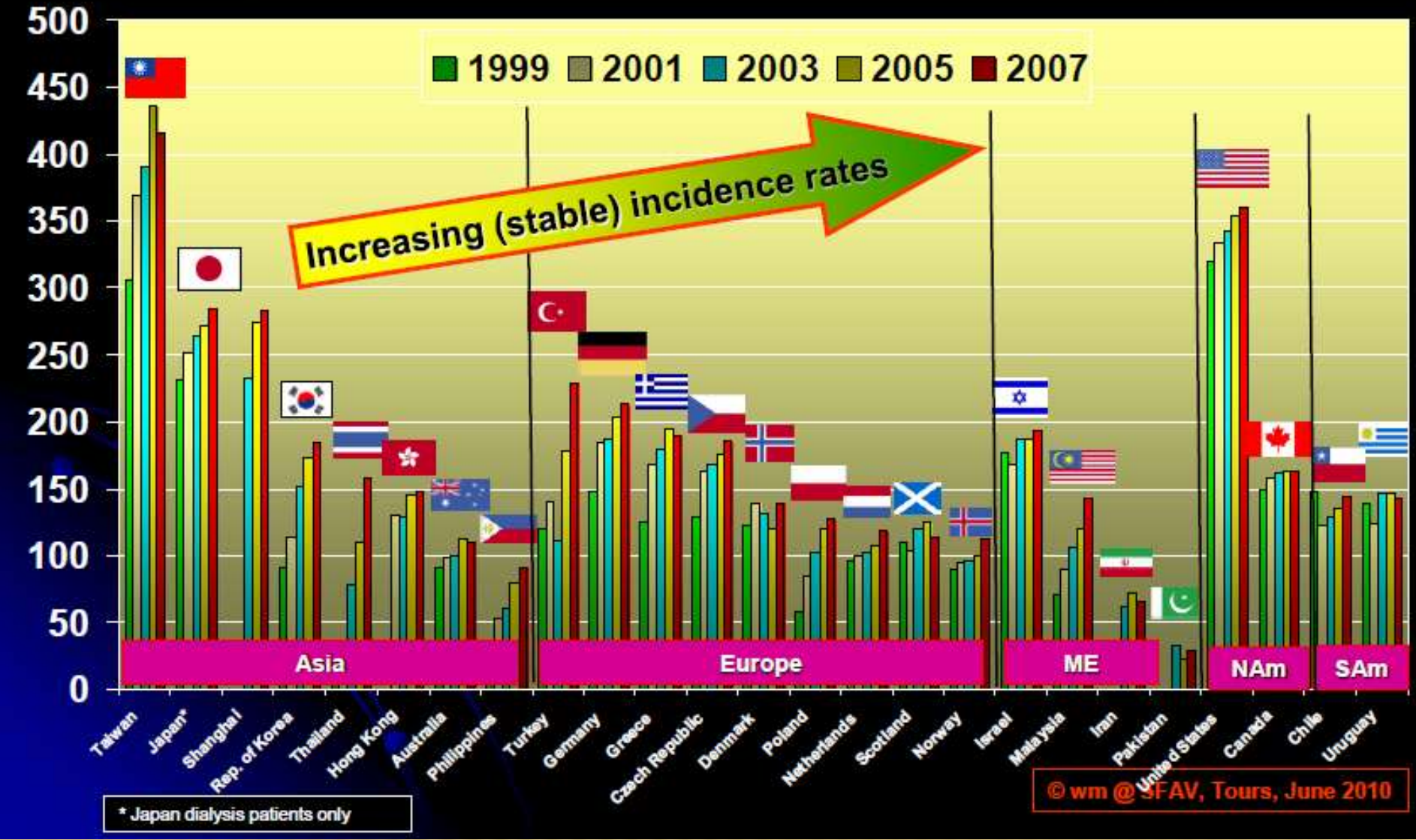
Summary CVD Risk In CKD



THE ESRD DILEMMA

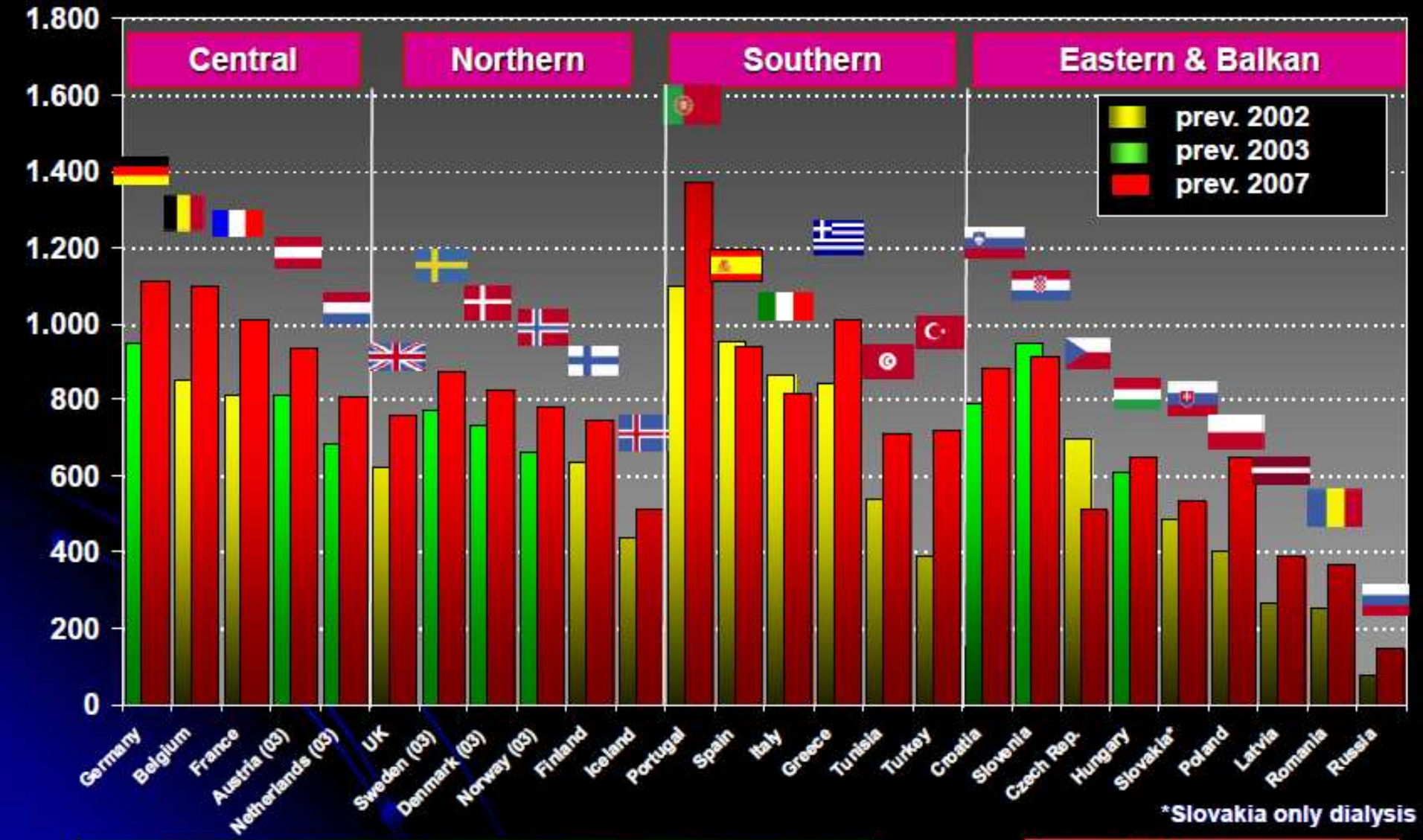
Trends in worldwide incidence rates (per million population - pmp)

selected countries from the USRDS-2009 report chapter 12



* Japan dialysis patients only

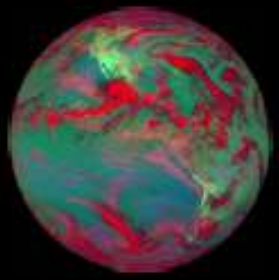
ESRD in Northern, Southern & Central & Eastern Europe
Prevalence (pmp) 2003 to 2007

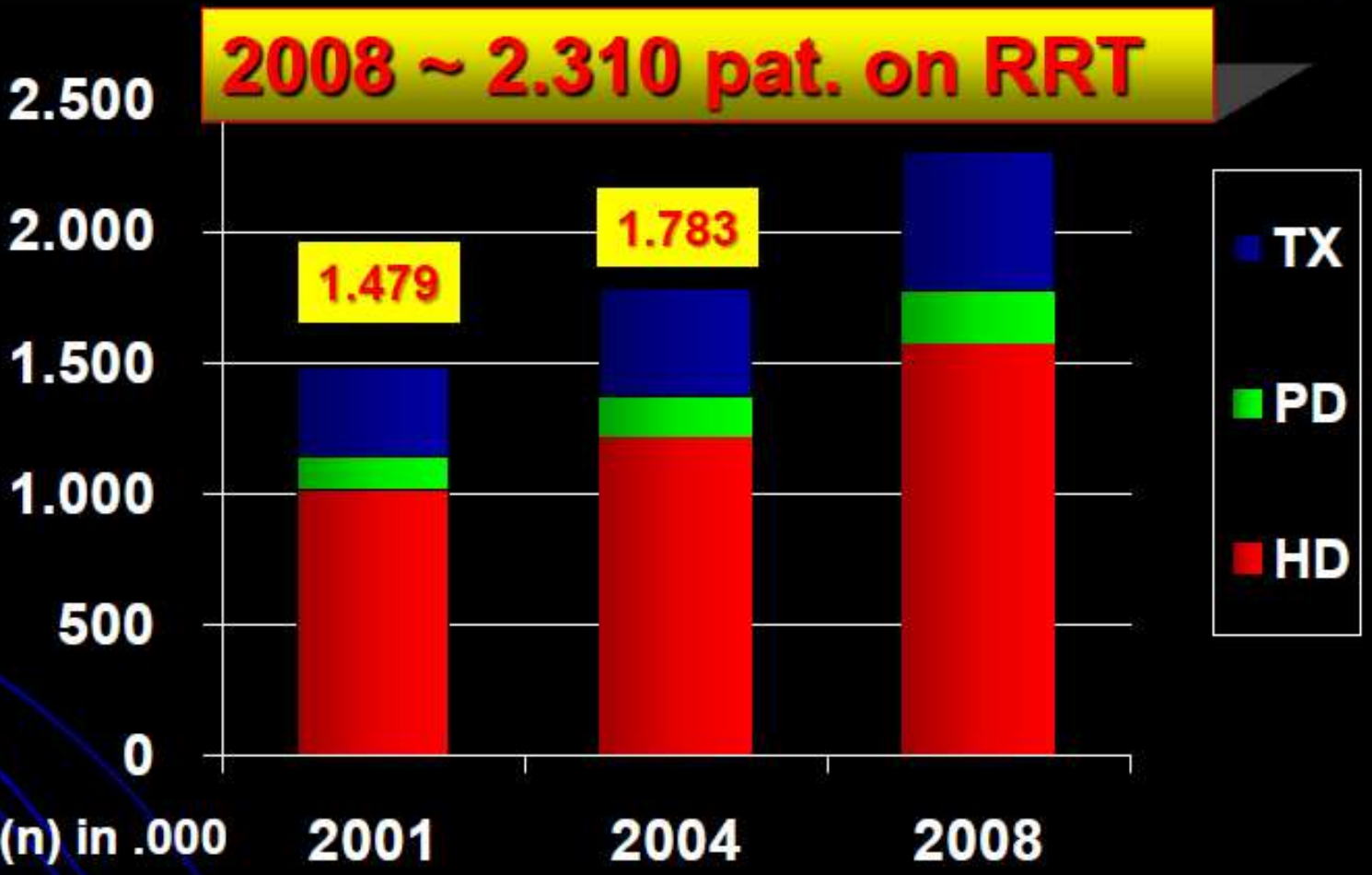


*Slovakia only dialysis

ERA-EDTA Registry Report 2002 and 2007 & National data

Worldwide ESRD / RRT – 2001 - 2008





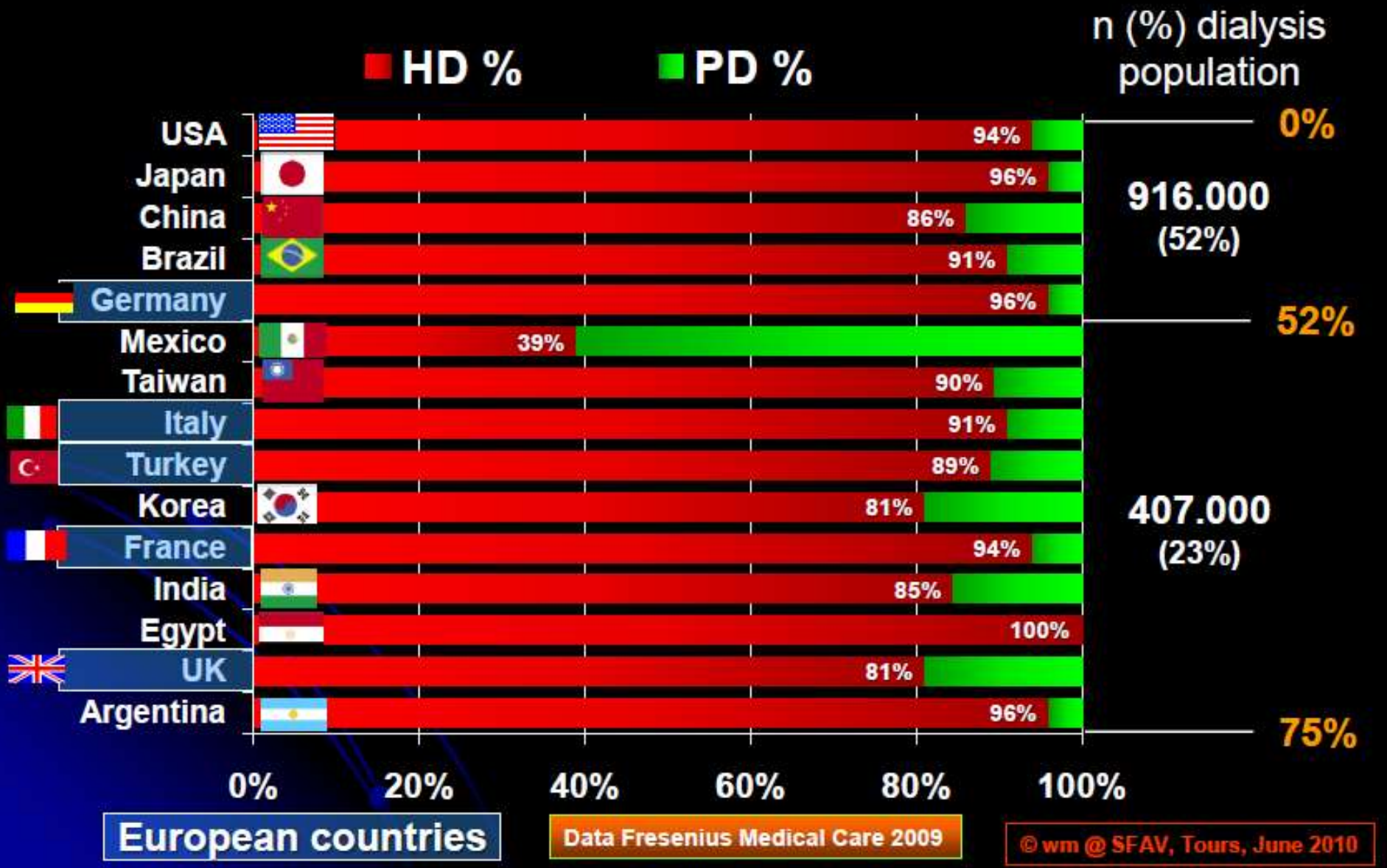
Moeller S, et al. Nephrol Dial Transplant 2002
Grassmann, NDT 2005
Fresenius Medical Care, 2009

Worldwide ESRD Treatment Modalities 2001 – 2008

No change in RRT treatment modality !

Moeller S, et al. NDT 2002
Grassmann, NDT 2005
Fresenius Medical Care, 2009

The 15 largest dialysis countries - HD vs PD



The Egyptian Renal Registry

9th Annual Report

2008

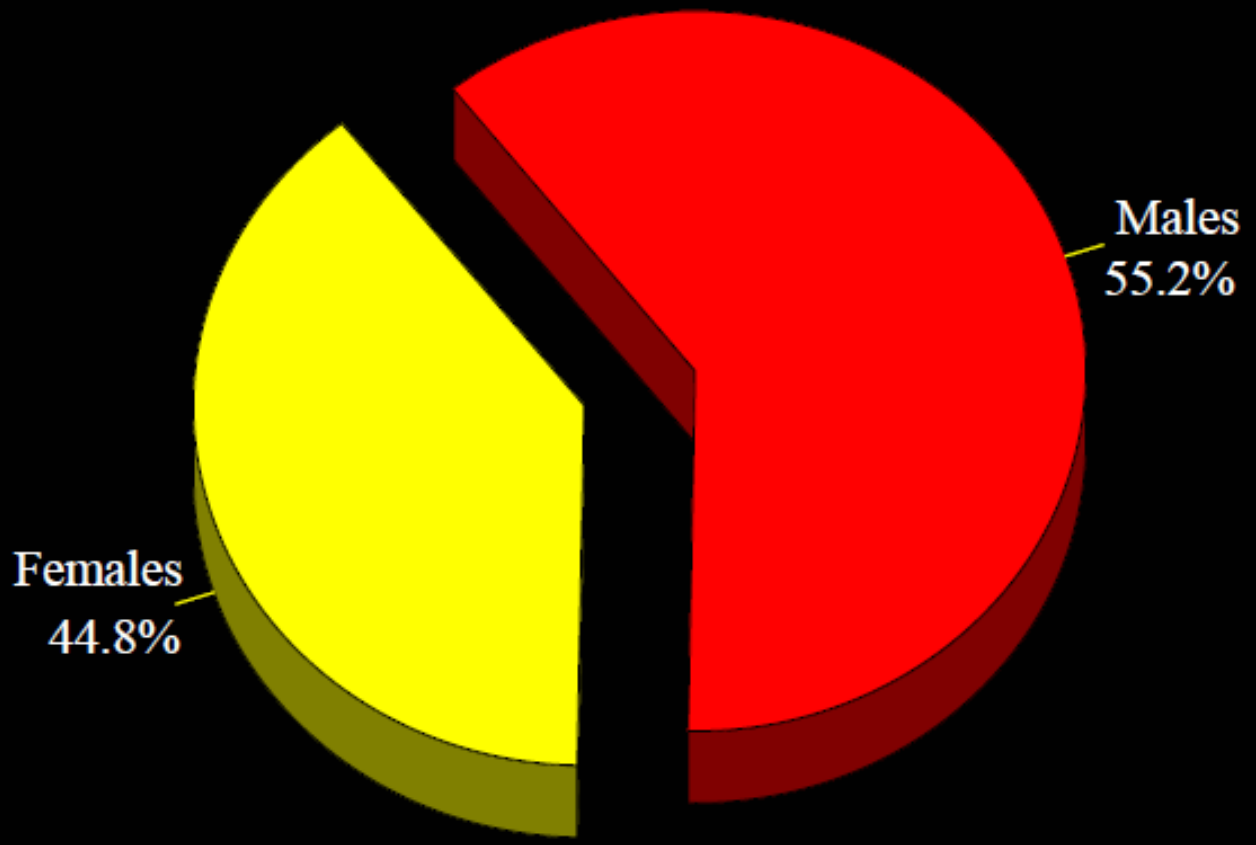
Adel Afifi, MD.

Professor of Internal Medicine & Nephrology

Ain Shams University, Cairo, Egypt

Gender distribution

n. 3550



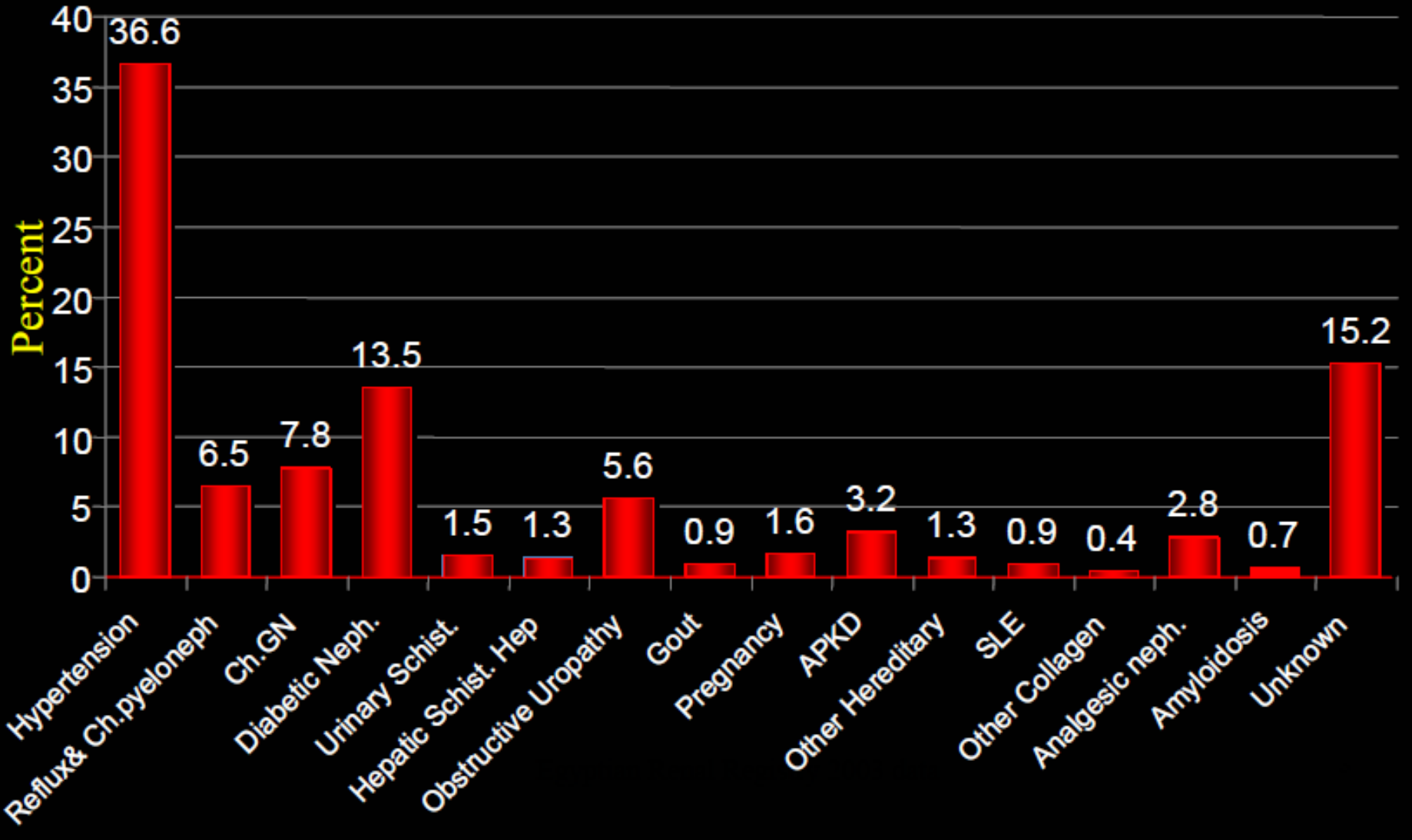
Mean age

n. 3453

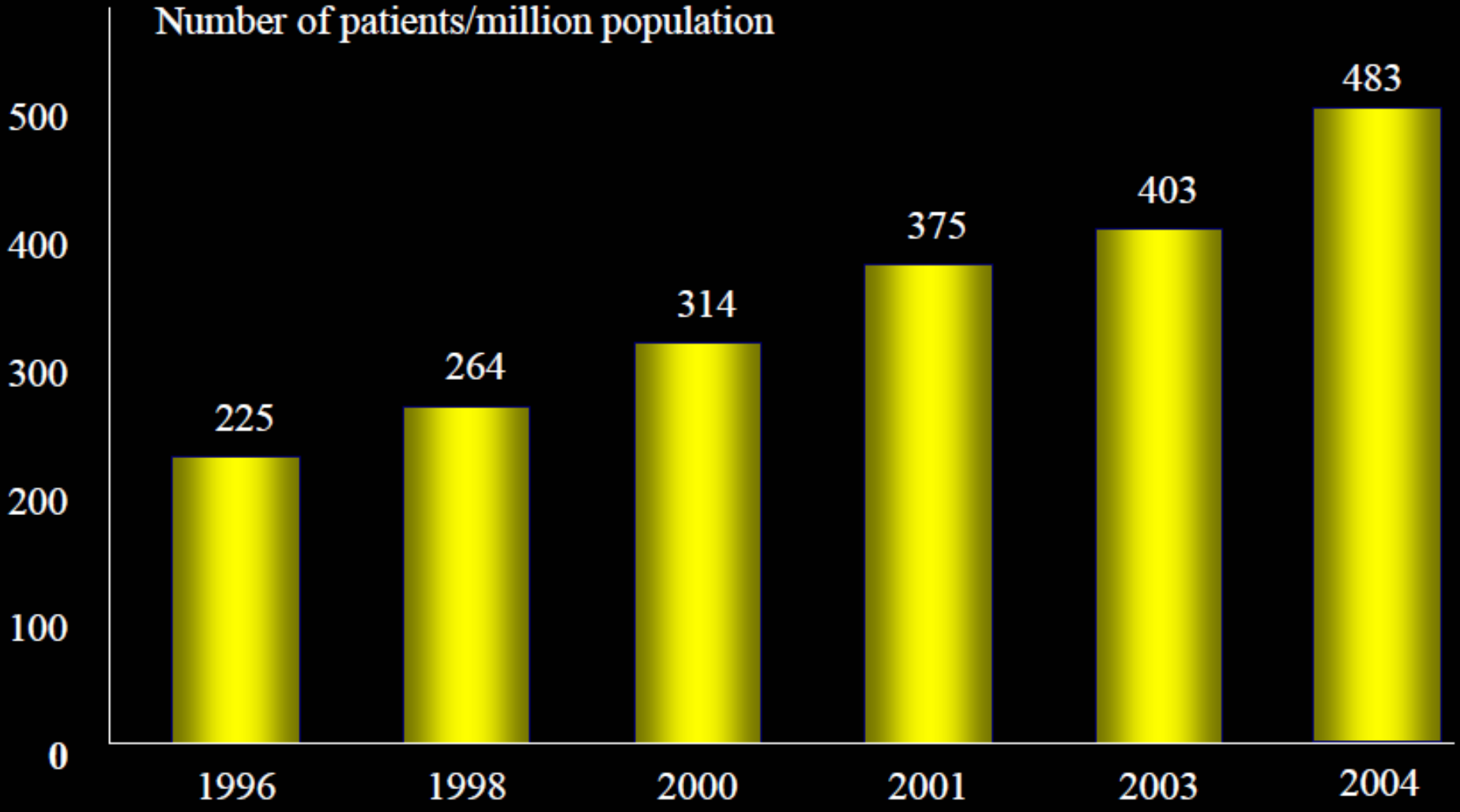
49.8 ± 19 years

Etiology of CKD

n. 2975



Prevalence of ESRD in Egypt



Social Consequences of RRT

- Dialysis
  - Performance at work
    - Days off work
    - Physical disability
    - Impaired cognitive functions

Periera et al. AJKD 2005;45: 448-462

Murray : Adv Chronic Kidney Dis. 2008;15:123-32

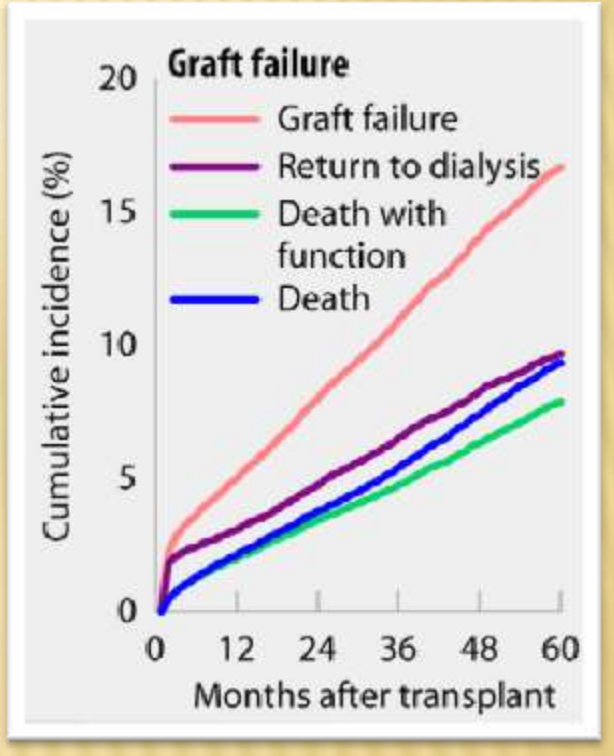
    - Impaired QOL

Arogundade & Barsoum. J Natl Med Assoc. 2004;96:1661-7.

  - Expenses
  - Transportation

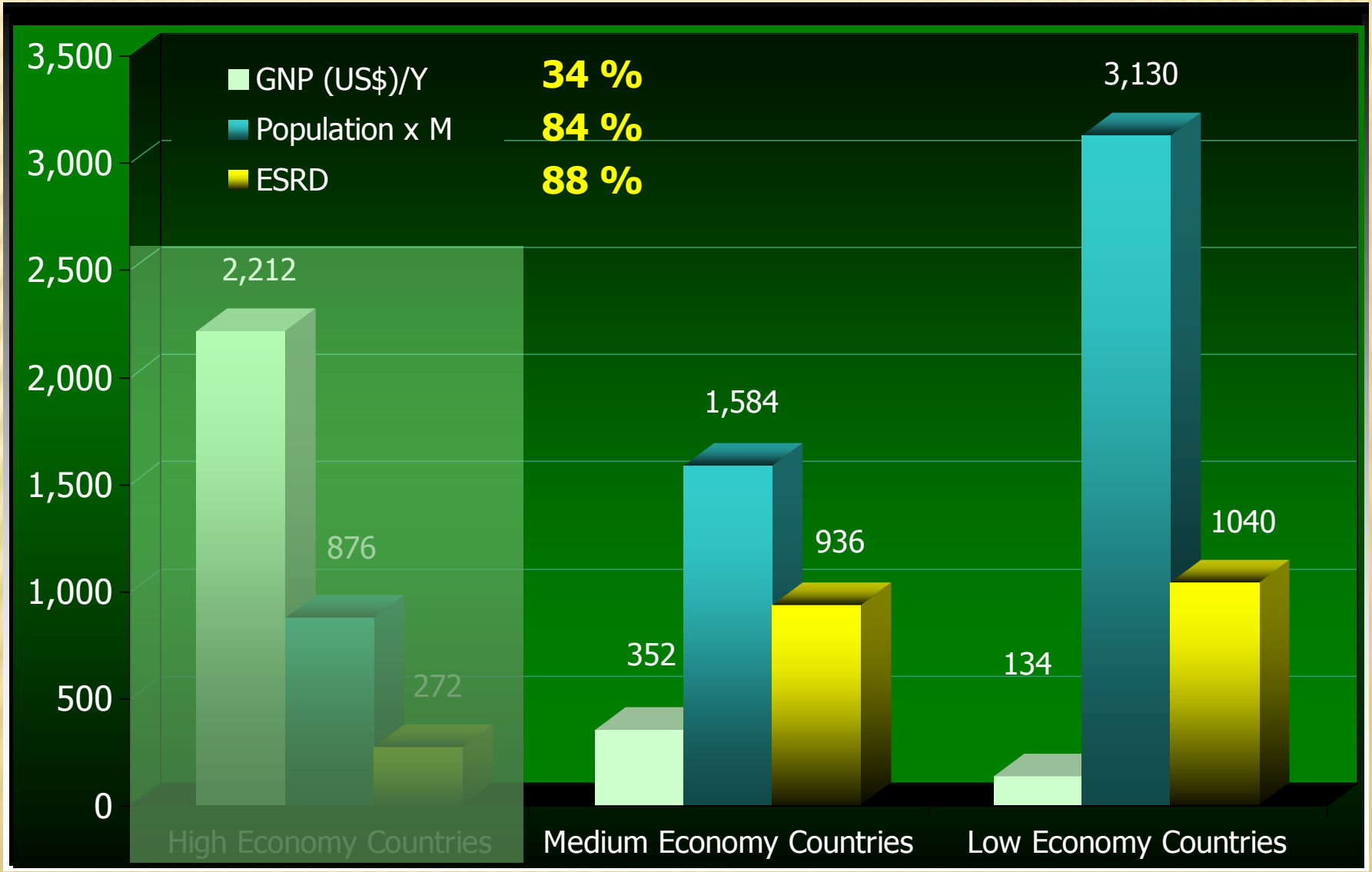
Social Consequences of RRT

- Transplantation
  - Donor issues
    - Related
      Farid et al. Med. J. Cairo Univ. 1996; 64 : 251-7
    - Unrelated
      - The dilemma of trafficking, commercialism etc.
        Delmonico & Dew. Kidney Int. 2007;71:608-14
      - Impaired long term performance
        Budiani, http://www.cofs.org/egypt.htm
    - Deceased
      - Legislation
      - Public response
      - Organization
  - Recipient issues
    - Expenses
    - Physical limitation
    - Long-term consequences



Live Donor

Economic Aspects of RRT



Barsoum . Artif Organs.2002 26:737-46

SCREENING OF CKD

International Recommendations for Targeted Screening for CKD

Targeted group	Guidelines			
	KDOQI	UK NICE	CARI	CSN
Elderly	•			
Hypertension	•	•	•	•
Diabetes mellitus	•	•	•	•
Atherosclerotic		•	•	•
Cardiovascular disease heart failure		•		•
Urologic disease, stone disease, recurrent urinary infections	•	•		
Systemic autoimmune conditions	•	•		•
Nephrotoxic drugs	•	•		•
High-risk ethnic groups	•		•	•
Family history of CKD	•	•		

Other high-risk groups may include smokers, metabolic syndrome, obesity, low birth weight, systemic infections, reduced renal mass, and previous acute kidney injury

ETIOLOGY OF CKD

- Multi-hit process.

- Risk factors for CKD:
  - Susceptibility factors: predispose to CKD,
  - Initiation factors: directly trigger kidney damage.
  - Progression factors: associated with worsening of already established kidney damage.

SUSCEPTIBILITY FACTORS

- Genetic and familial predisposition.
- Race (Afro-Caribbeans, Indo-Asians).
- Maternalfetal factors (low birth weight, malnutrition in utero).
- age (elderly).
- gender (male).

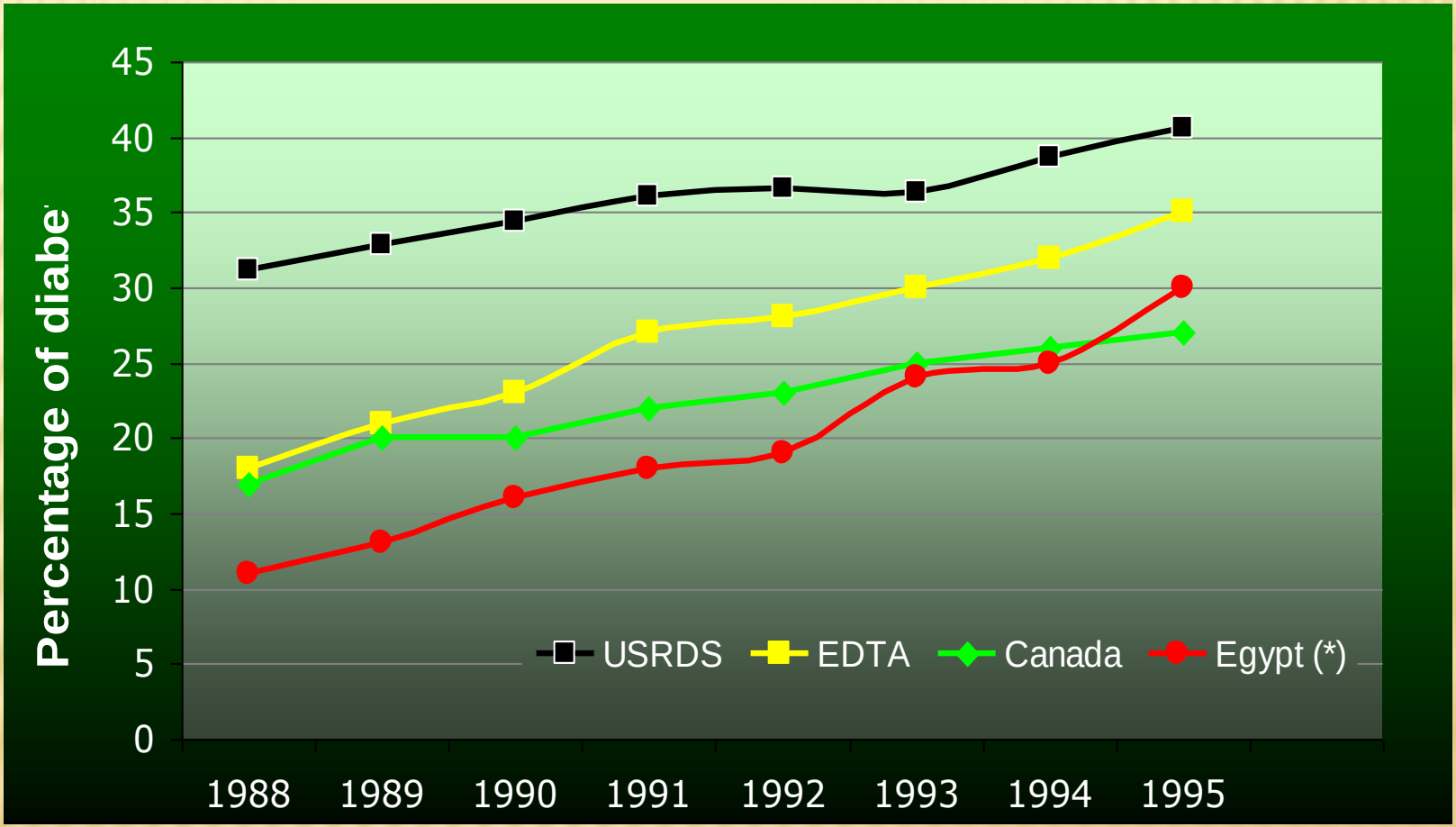
INITIATION FACTORS

- Diabetes Mellitus
- Hypertension
- Glomerulonephritis
- Interstitial nephritis
- Cystic renal diseases
- Others:
  - Obesity/metabolic syndrome
  - Hyperuricemia
  - Cardiovascular disease
  - Smoking
  - Nephrotoxins exposure: NSAIDs.

DIABETES MELLITUS

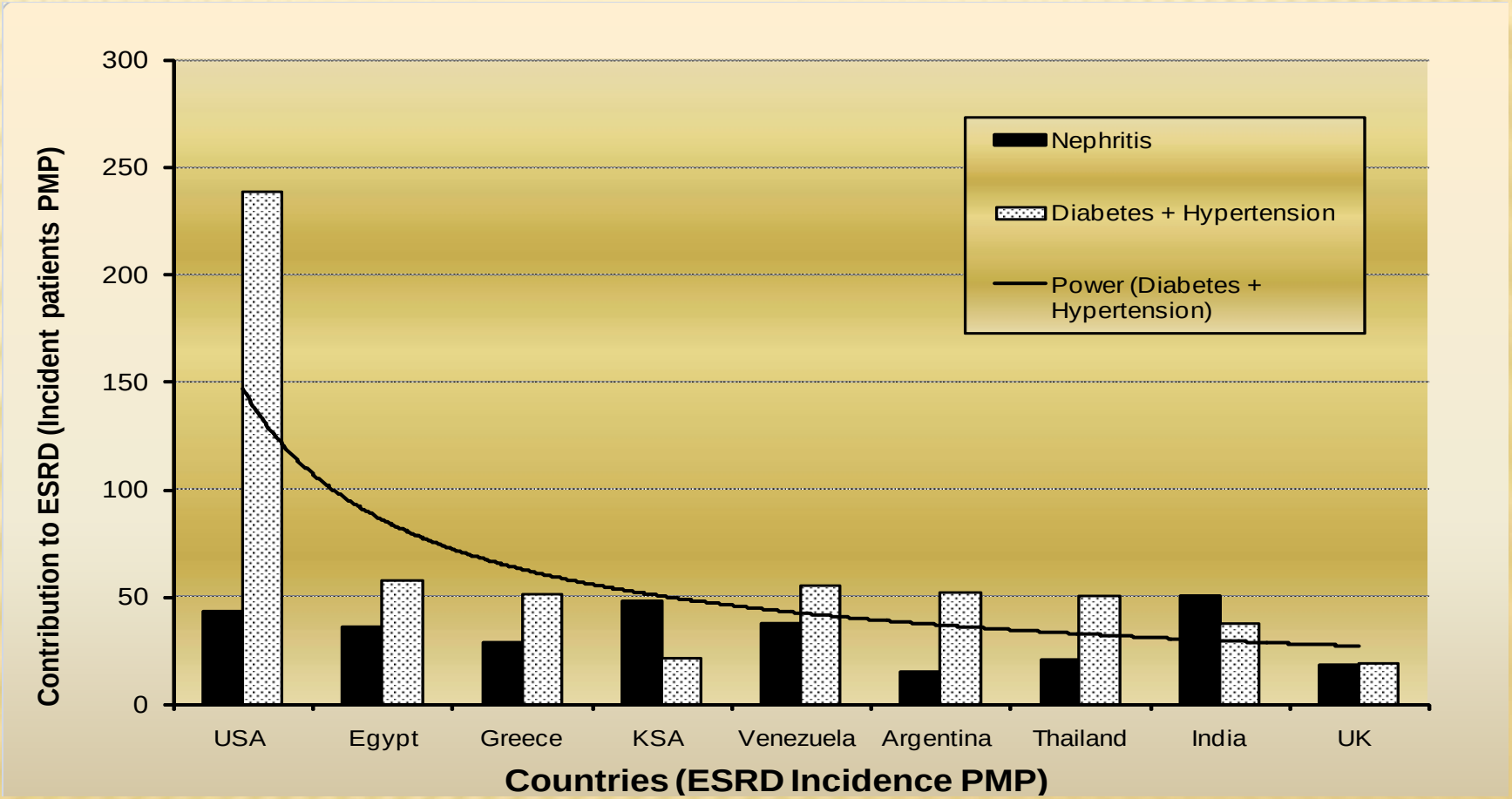
- Diabetic nephropathy (DN)
- Diabetic renal vascular disease (DRVD)
- Bladder autonomic dysfunction
- Recurrent UTI
- Papillary necrosis
- Nephrotoxicity: e.g. radiocontrast media
- Infections

Historical Role Of Diabetes



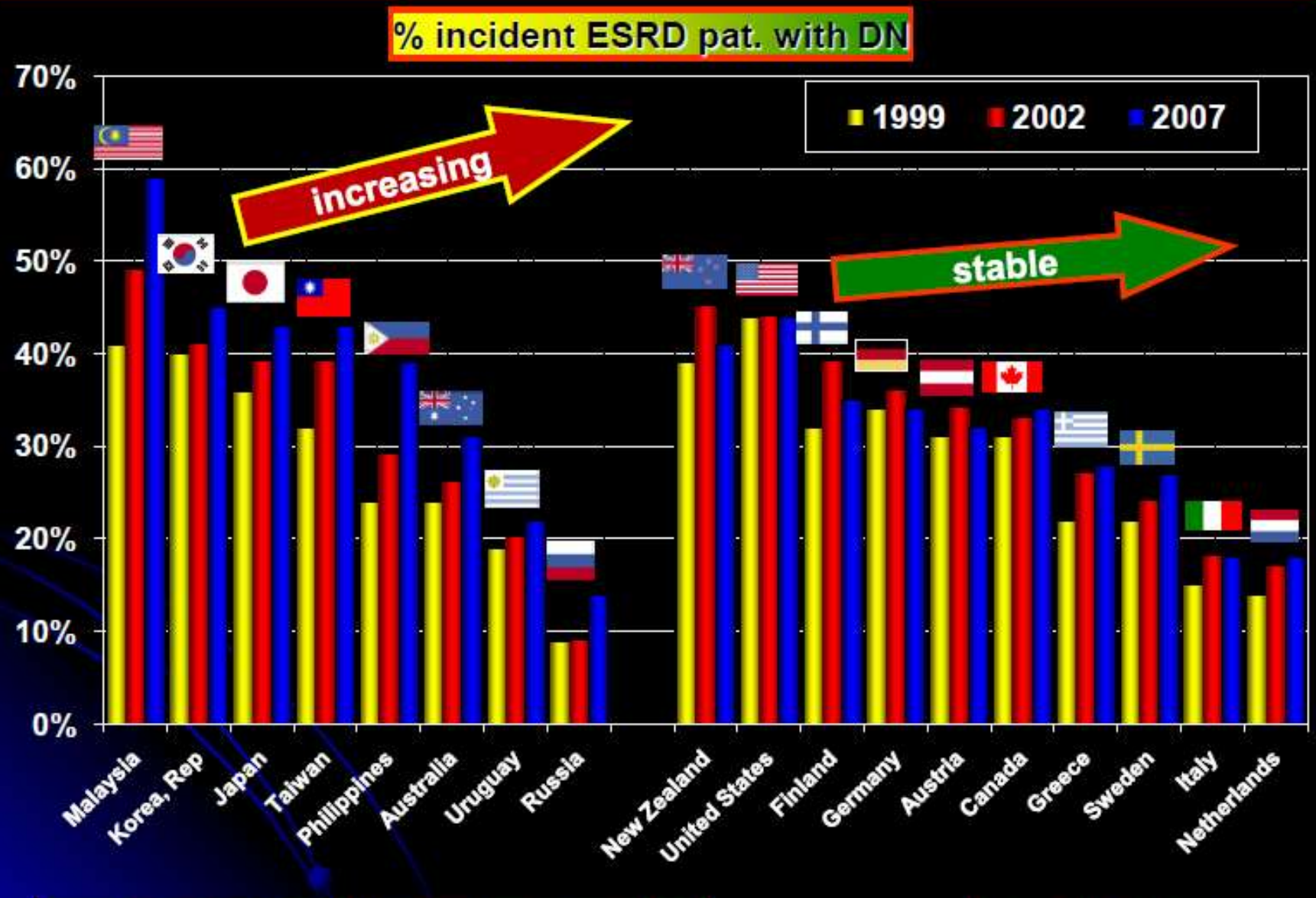
Constructed from multiple registry data

Current Role Of Diabetes



Adapted from Barsoum, Artif Organs 2002 ;26:735-6

Trends in worldwide incidence rates of Diabetic Nephropathy (DN)



selected countries from the USRDS-2009 report chapter 12

Trends in Diabetic disease worldwide 2000 to 2030

366 Mill. diabetics in 2030

+ 195 Mill.

171 Mill. diabetics in 2000

+114 %

World Health Organization

http://www.who.int/diabetes/facts/world_figures/en/

World Wide Diabetes Map 2000 ➡ 2030

Wild S Diabetes Care (2004) 27:1047–1053
http://www.who.int/diabetes/facts/en/

Top Ten Countries With Highest Prevalence Of Diabetes

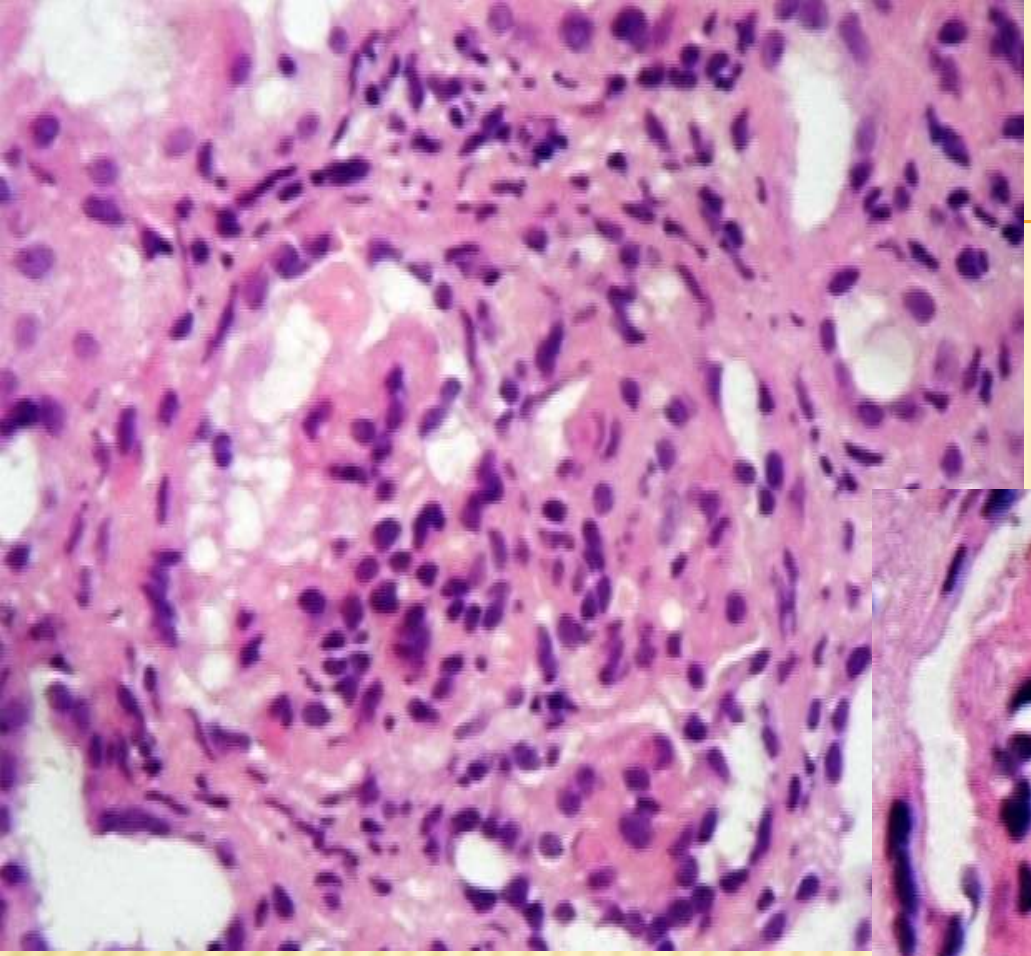
Table 3 —*List of countries with the highest numbers of estimated cases of diabetes for 2000 and 2030*

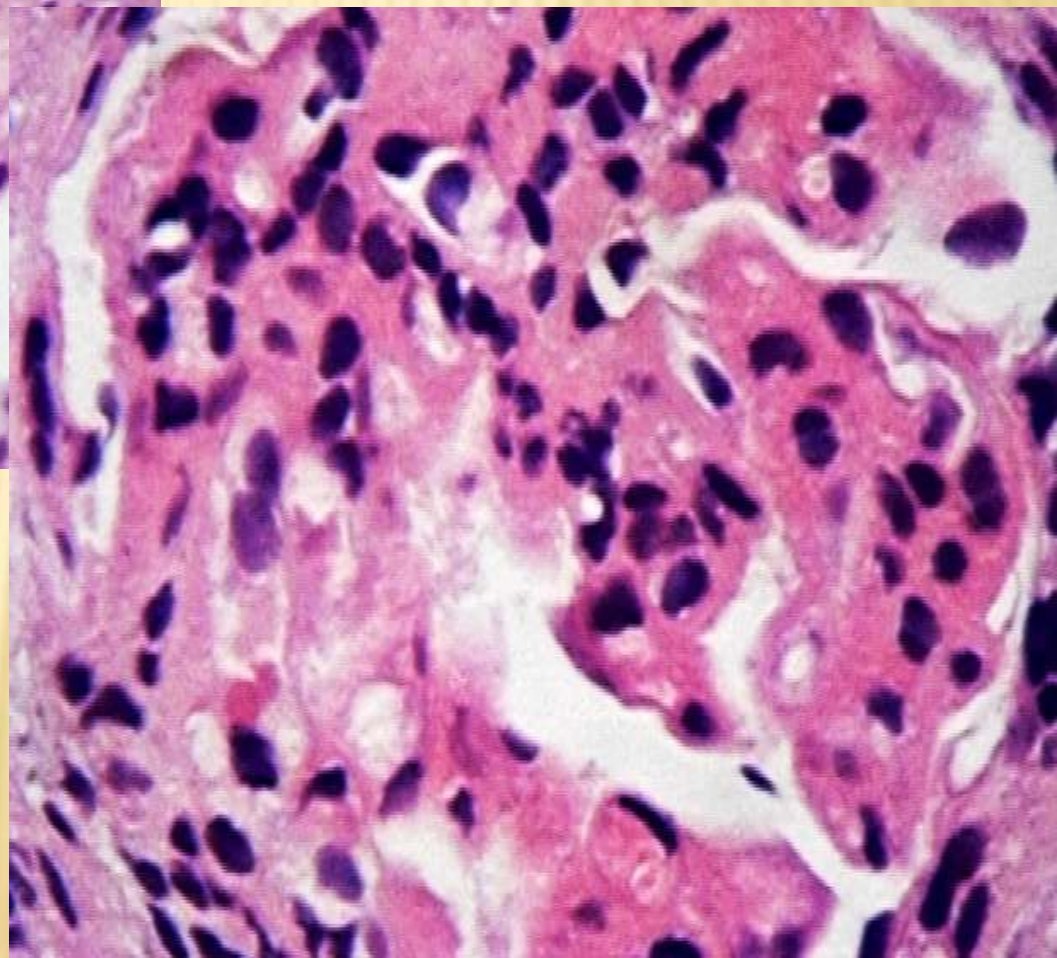
	2000		2030	
Ranking	Country	People with diabetes (millions)	Country	People with diabetes (millions)
1	India	31.7	India	79.4
2	China	20.8	China	42.3
3	U.S.	17.7	U.S.	30.3
4	Indonesia	8.4	Indonesia	21.3
5	Japan	6.8	Pakistan	13.9
6	Pakistan	5.2	Brazil	11.3
7	Russian Federation	4.6	Bangladesh	11.1
8	Brazil	4.6	Japan	8.9
9	Italy	4.3	Philippines	7.8
10	Bangladesh	3.2	Egypt	6.7

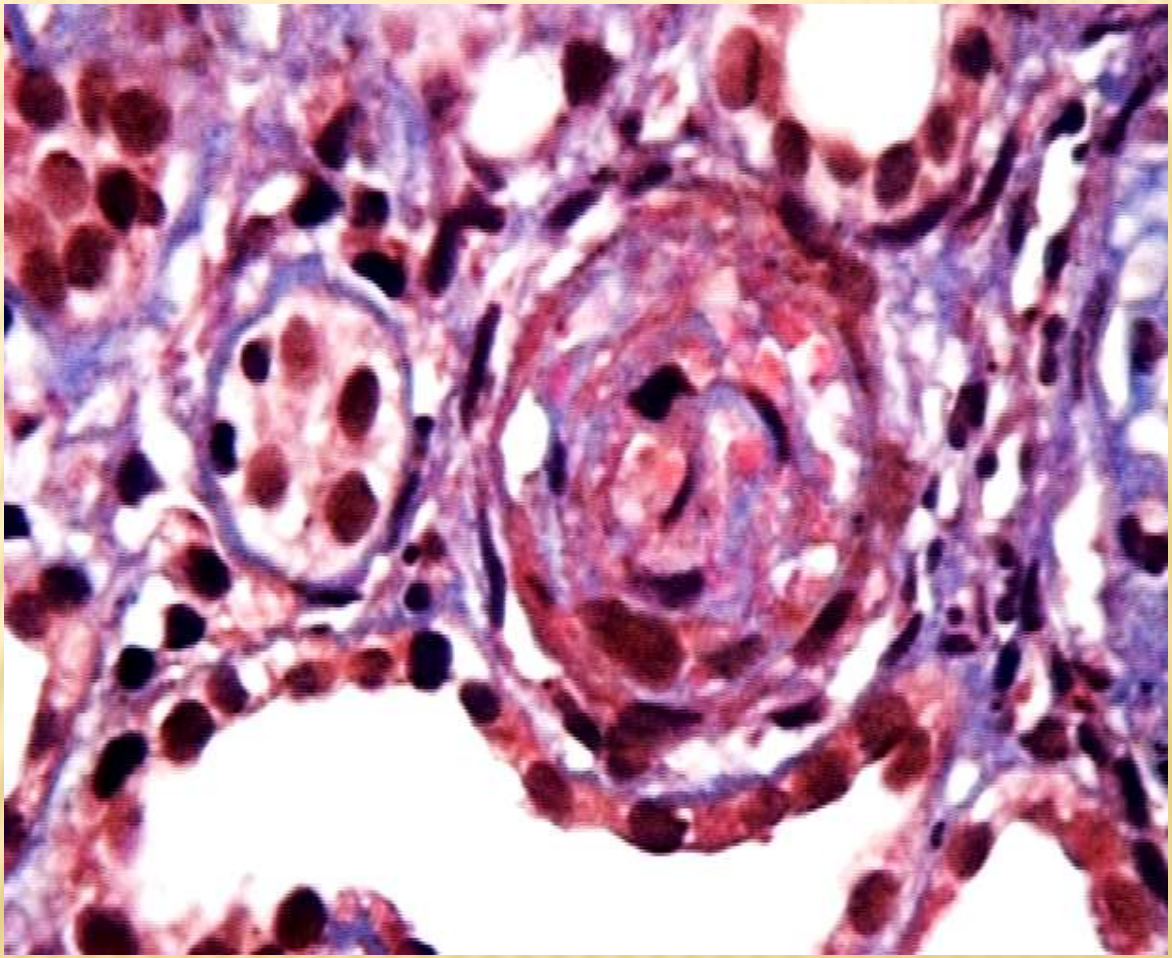
Wild et al. Diabetes Care 2004;27:1047-1053

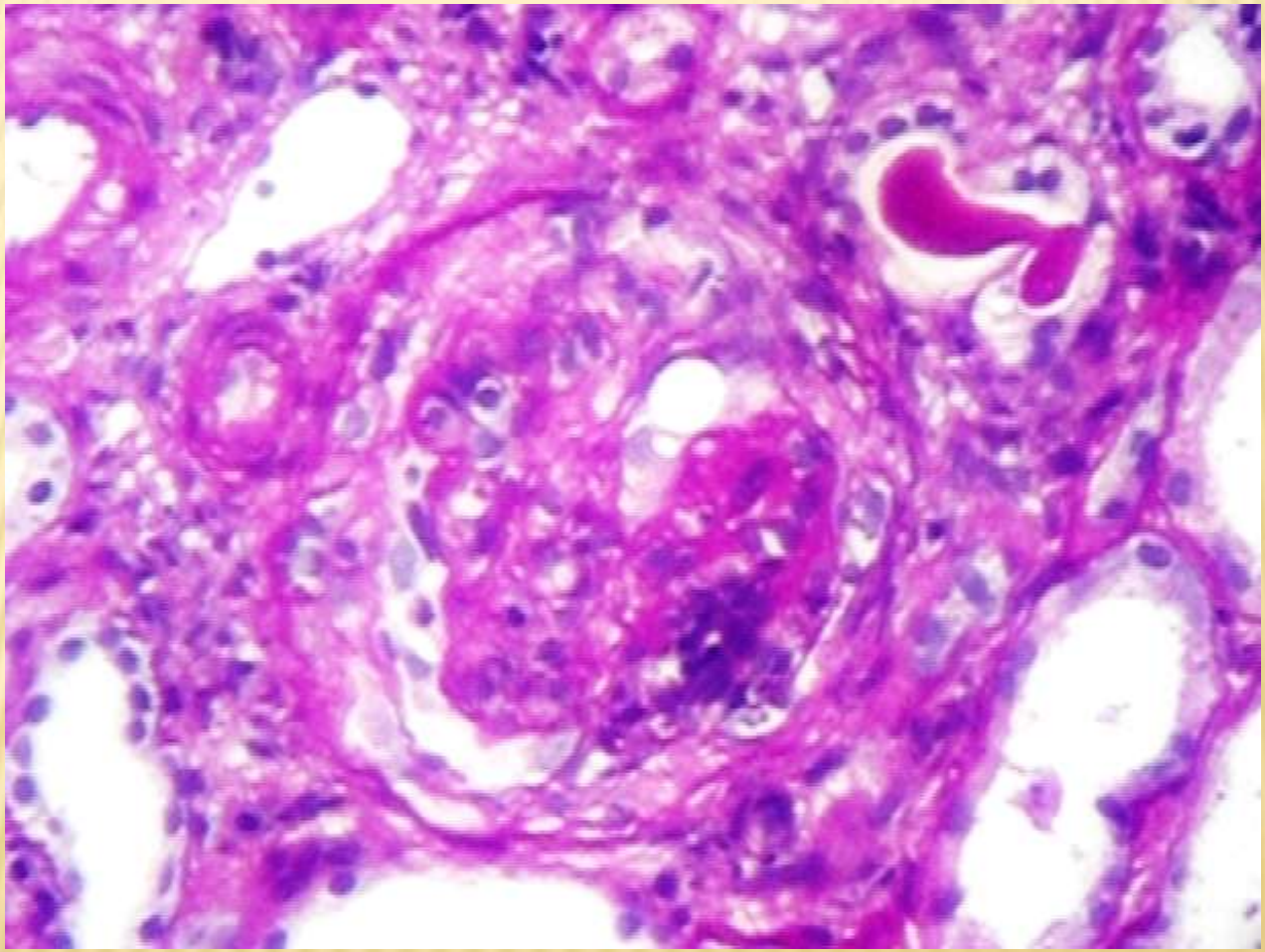
FINAL MESSAGE

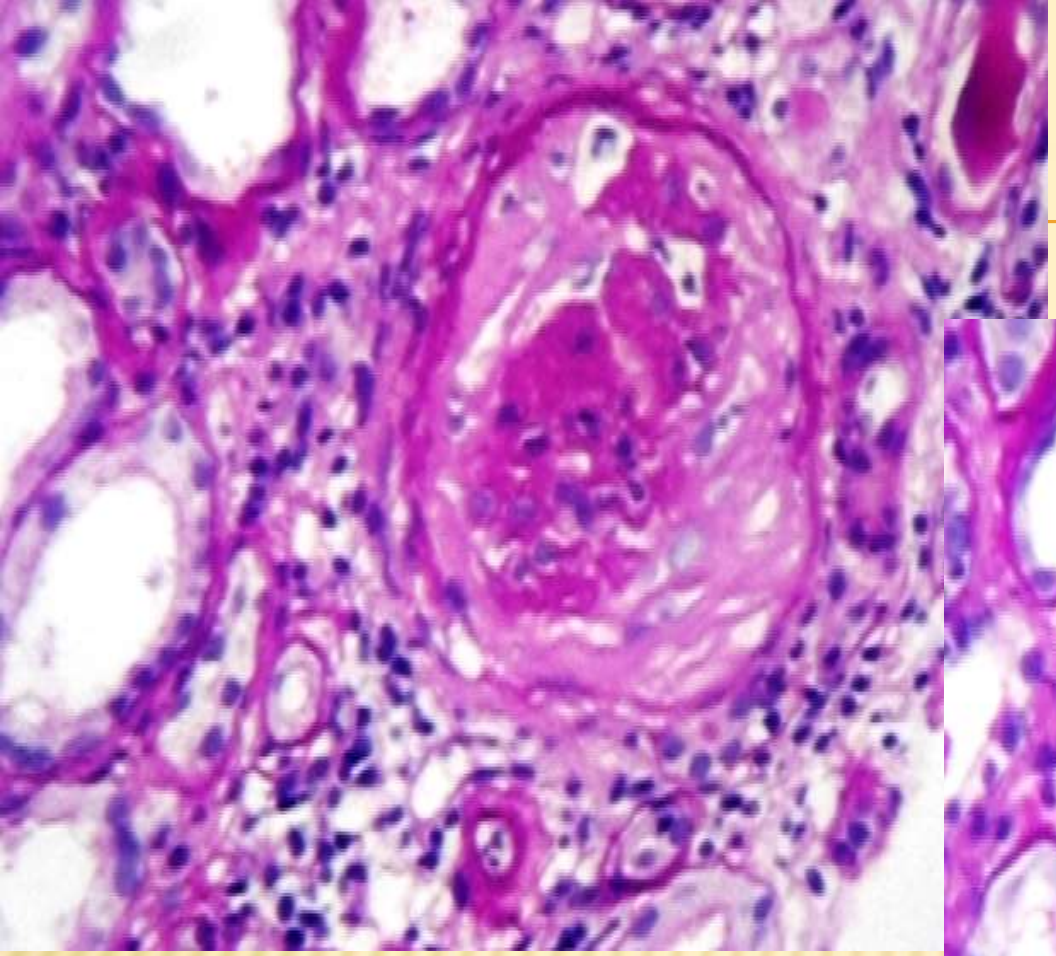
- 19 –year- female, Aswan
- Anemia 1 year ago, oral iron
- Creat. 19 mg/dl
- Urine: prot. +++, Prot/creat ratio 3 gm/gm
- Renal US: normal
- Hb: 5.5 NN
- Comb's test: Direct +ve
- ESR: 125 / 140
- Echo: thin rim of pericardial effusion
- ANA, Anti dsDNA, RF, ANCA-c & virology: -ve
- ANCA-p: weak +ve

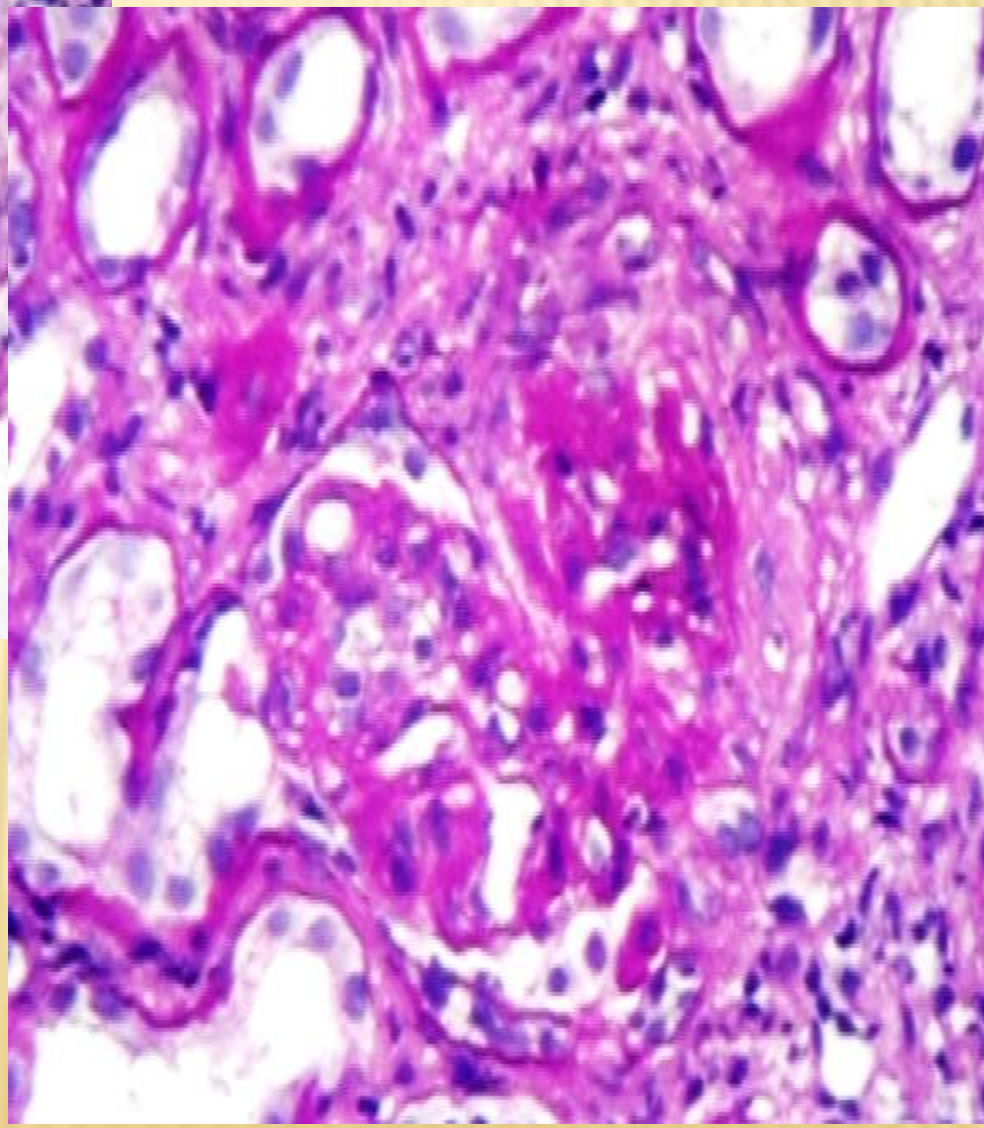


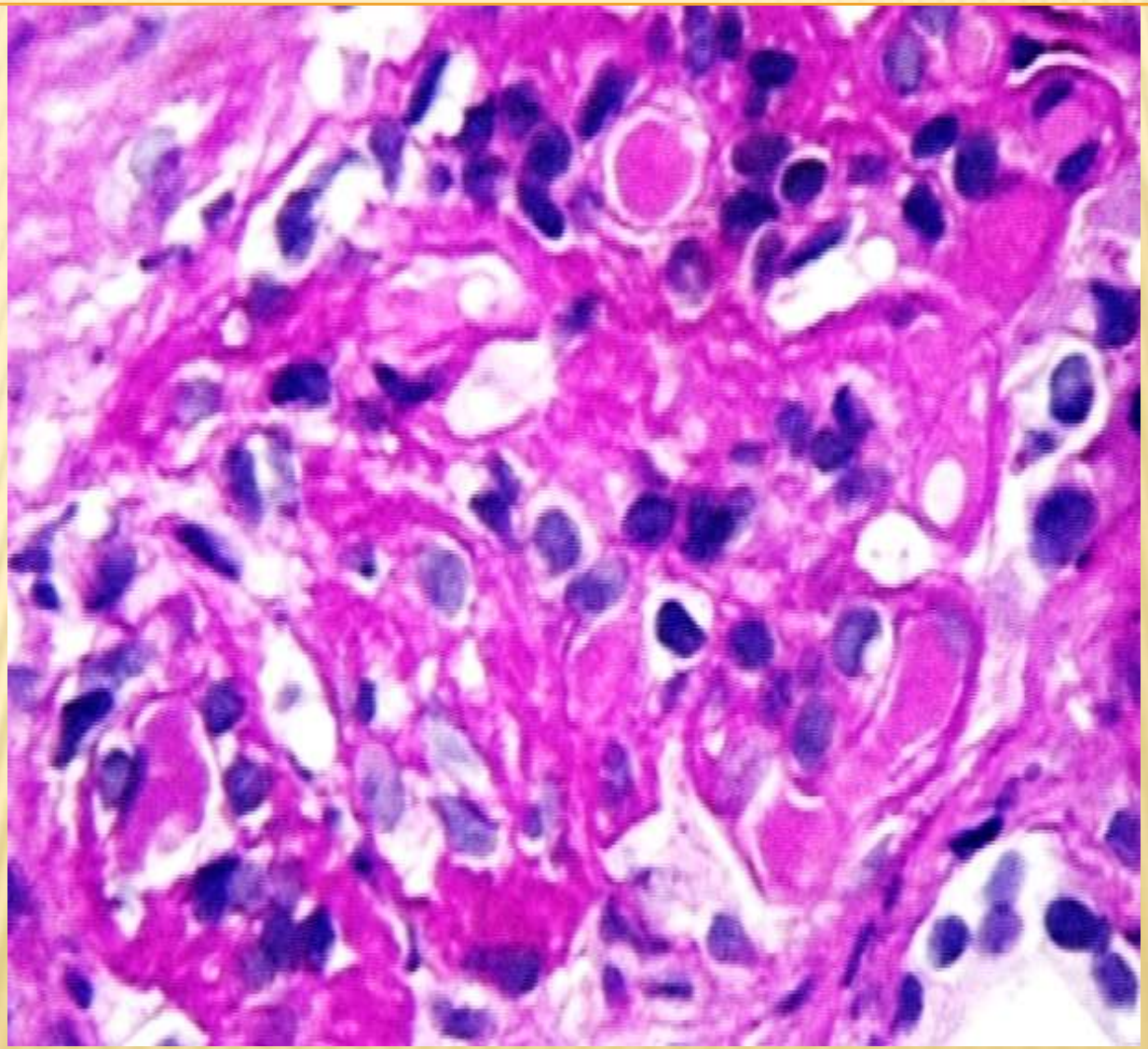








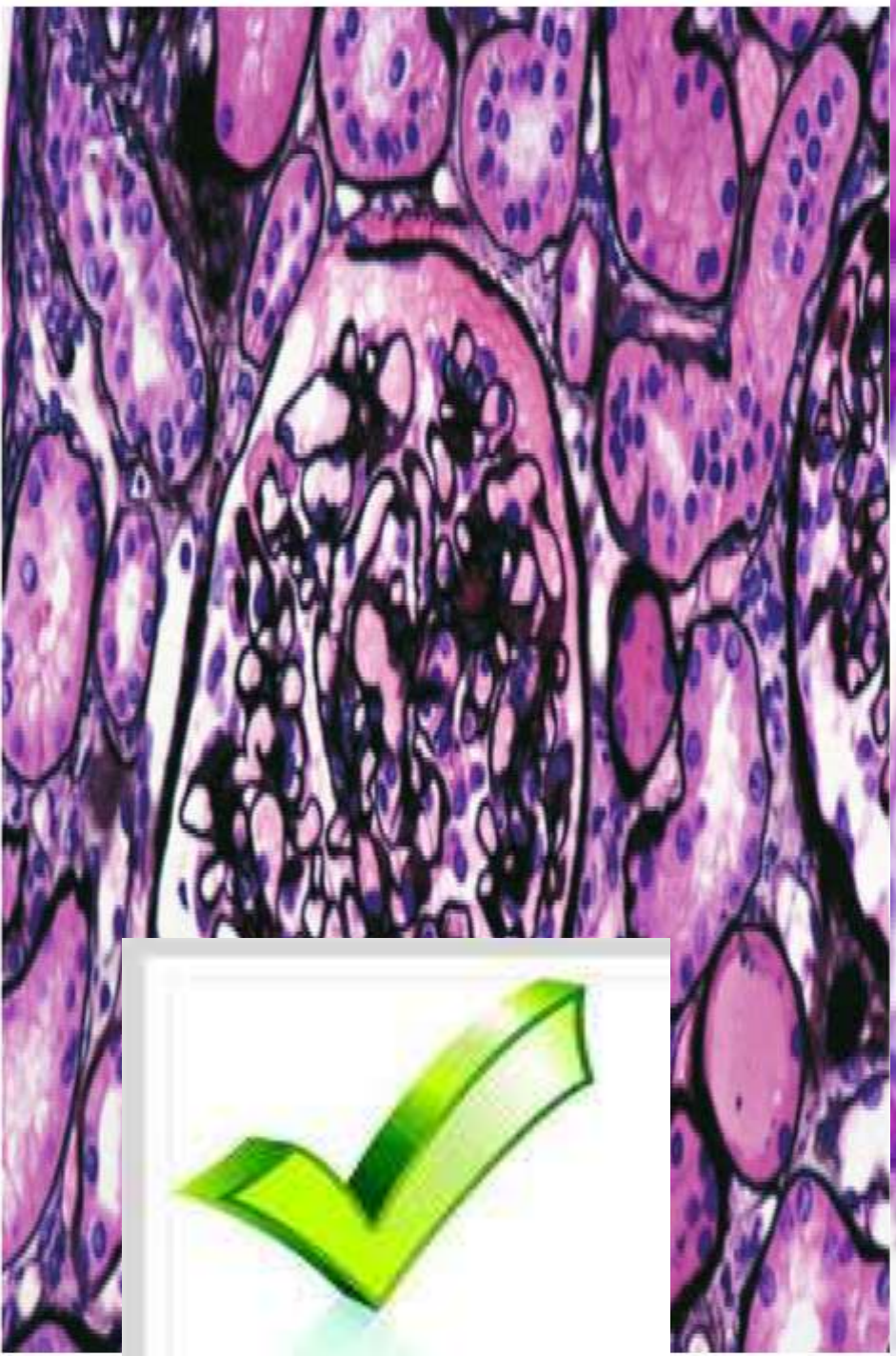


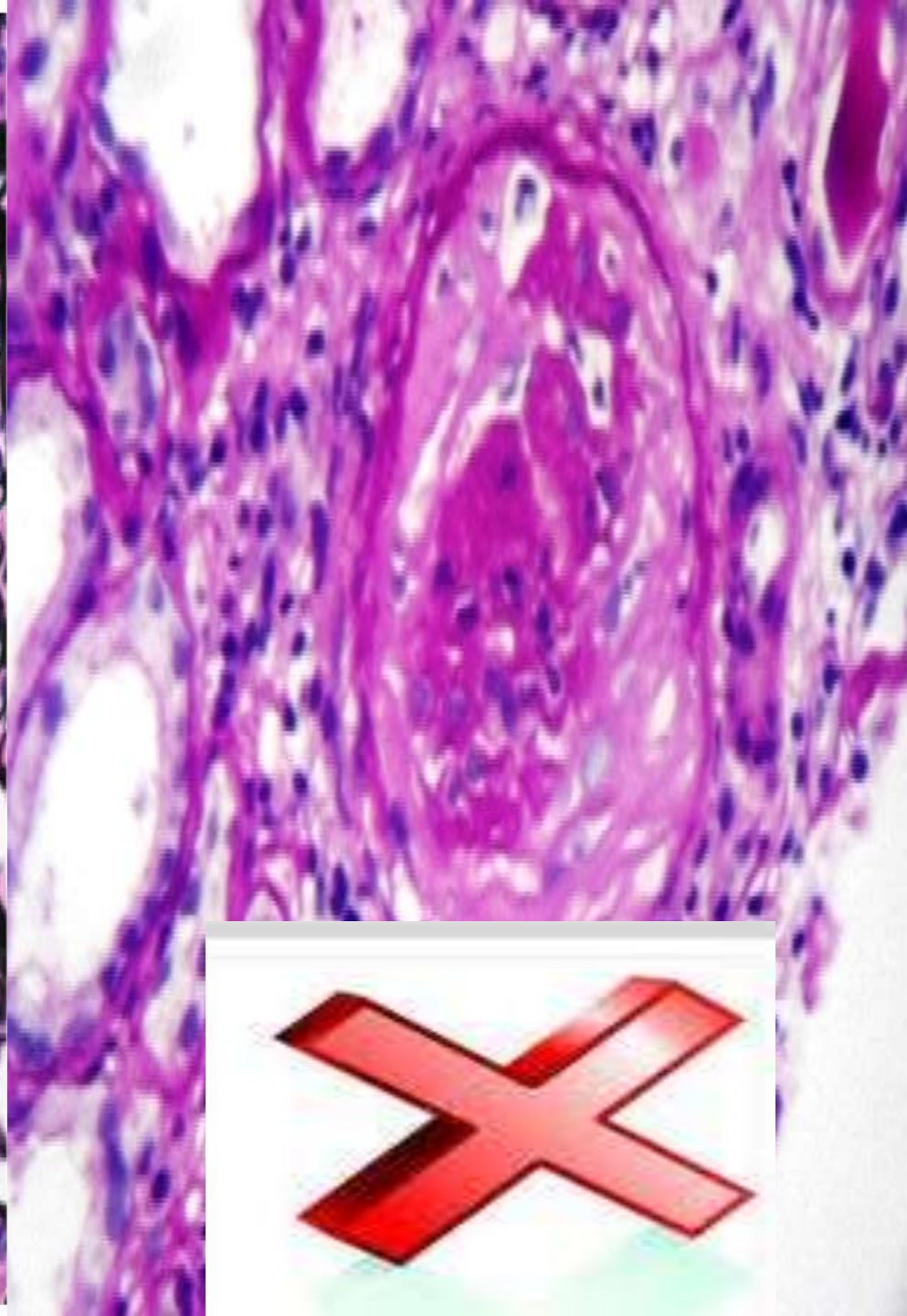


SUSPECT CKD & TREAT EARLY

- Underlying disease:
  - DM
  - HTN
  - Excessive obesity
  - Endemic infection

- Mistaken manifestations of CKD:
  - Anemia
  - GIT disorders
  - Premature CVD






Thank you